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 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2          "Ask CAS" for self-help around the clock
 NEWS  3  Jul 12  BEILSTEIN enhanced with new display and select
options,
                  resulting in a closer connection to BABS
 NEWS  4  AUG 02  IFIPAT/IFIUDB/IFICDB reloaded with new search and
display
                  fields
 NEWS  5  AUG 02  CAplus and CA patent records enhanced with European
and Japan
                  Patent Office Classifications
 NEWS  6  AUG 02  The Analysis Edition of STN Express with Discover!
                  (Version 7.01 for Windows) now available
 NEWS  7  AUG 27  BIOCOMMERCE: Changes and enhancements to content
coverage
 NEWS  8  AUG 27  BIOTECHABS/BIOTECHDS: Two new display fields added
for legal
                  status data from INPADOC
 NEWS  9  SEP 01  INPADOC: New family current-awareness alert (SDI)
available
 NEWS 10  SEP 01  New pricing for the Save Answers for SciFinder
Wizard within
                  STN Express with Discover!
 NEWS 11  SEP 01  New display format, HITSTR, available in
WPIDS/WPINDEX/WPIX
 NEWS 12  SEP 27  STANDARDS will no longer be available on STN
 NEWS 13  SEP 27  SWETSCAN will no longer be available on STN

 NEWS EXPRESS  JULY 30 CURRENT WINDOWS VERSION IS V7.01, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to
STN
 NEWS WWW      CAS World Wide Web Site (general information)

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* *

FILE 'HOME' ENTERED AT 14:24:22 ON 26 OCT 2004

=> index biosci
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS                                SINCE FILE
TOTAL
                                                      ENTRY
SESSION
FULL ESTIMATED COST                                    0.42
0.42

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE,
AQUALINE,
      AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS, BIOTECHABS,
BIOTECHDS,
      BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN,
CONFSCI, CROPB,
      CROPU, DDFB, DDFU, DGENE, DISSABS, ...' ENTERED AT 14:25:23 ON
26 OCT 2004

75 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> fil reg
COST IN U.S. DOLLARS                                SINCE FILE
TOTAL
                                                      ENTRY
SESSION
FULL ESTIMATED COST                                    1.14
1.56

FILE 'REGISTRY' ENTERED AT 14:26:32 ON 26 OCT 2004
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STRUCTURE FILE UPDATES:   25 OCT 2004  HIGHEST RN 769101-30-6
DICTIONARY FILE UPDATES:  25 OCT 2004  HIGHEST RN 769101-30-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

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details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> S 300832-84-2/RN
L1             1 300832-84-2/RN

=> DEL SEL Y

=> SEL RN
E1 THROUGH E1 ASSIGNED

=> INDEX BEILSTEIN, GMELIN
COST IN U.S. DOLLARS                                SINCE FILE
TOTAL
                                                      ENTRY
SESSION
FULL ESTIMATED COST                                    0.92
2.48

INDEX 'BEILSTEIN, GMELIN' ENTERED AT 14:27:43 ON 26 OCT 2004

2 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> S E1 AND OPTICAL?/FA
FILE 'BEILSTEIN'
             0 300832-84-2/BI
               (300832-84-2/RN)
        753186 OPTICAL?/FA
             0 300832-84-2/BI AND OPTICAL?/FA
FILE 'GMELIN'
             0 300832-84-2/BI
               (300832-84-2/RN)
         12899 OPTICAL?/FA
             0 300832-84-2/BI AND OPTICAL?/FA

L2   QUE 300832-84-2/BI AND OPTICAL?/FA

=> DIS RANK
NO F-NUMBERS HAD GREATER THAN ZERO HITS


=> FIL CAPLUS
COST IN U.S. DOLLARS                                SINCE FILE
TOTAL
                                                      ENTRY
SESSION
FULL ESTIMATED COST                                    0.57
3.05

FILE 'CAPLUS' ENTERED AT 14:28:02 ON 26 OCT 2004
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FILE COVERS 1907 - 26 Oct 2004  VOL 141 ISS 18
FILE LAST UPDATED: 25 Oct 2004  (20041025/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> S L1/BMF
            15 L1
         52155 BMF/RL
L3           0 L1/BMF
               (L1 (L) BMF/RL)

=> FIL CAPLUS
COST IN U.S. DOLLARS                                SINCE FILE
TOTAL
                                                      ENTRY
SESSION
FULL ESTIMATED COST                                    2.26
5.31

FILE 'CAPLUS' ENTERED AT 14:28:18 ON 26 OCT 2004
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FILE COVERS 1907 - 26 Oct 2004 VOL 141 ISS 18
FILE LAST UPDATED: 25 Oct 2004 (20041025/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S L1/BPN
15 L1
102210 BPN/RL
L4 0 L1/BPN
(L1 (L) BPN/RL)

=> FIL CAPLUS
COST IN U.S. DOLLARS SINCE FILE
TOTAL
ENTRY
SESSION
FULL ESTIMATED COST 2.26
7.57

FILE 'CAPLUS' ENTERED AT 14:28:28 ON 26 OCT 2004
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FILE COVERS 1907 - 26 Oct 2004 VOL 141 ISS 18
FILE LAST UPDATED: 25 Oct 2004 (20041025/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S L1/IMF
15 L1
390491 IMF/RL
L5 0 L1/IMF
(L1 (L) IMF/RL)

=> FIL CAPLUS
COST IN U.S. DOLLARS SINCE FILE
TOTAL
ENTRY
SESSION
FULL ESTIMATED COST 2.26
9.83

FILE 'CAPLUS' ENTERED AT 14:28:41 ON 26 OCT 2004
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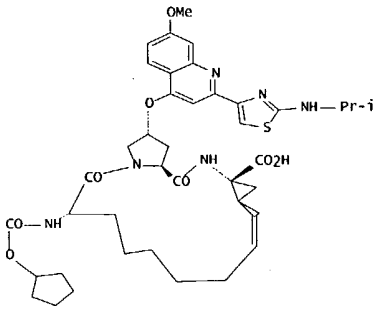
FILE COVERS 1907 - 26 Oct 2004 VOL 141 ISS 18
FILE LAST UPDATED: 25 Oct 2004 (20041025/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S L1/PEP
15 L1
1687596 PEP/RL
L6 1 L1/PEP
(L1 (L) PEP/RL)

=> DIS L6 1 CBIB ABS HITRN

L6 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
2004:310970 Document No. 140:327091 Potent inhibitor of HCV serine protease.
Chen, Shirlynn; Nehmiz, Gerhard; Croenlein, Jens Oliver; Steinmann,
Gerhard; Gunn, Jocelyn Abella; Costa, Phuong Do (Boehringer Ingelheim
International G.m.b.H., Germany). PCT Int. Appl. WO 2004030670 A1
20040415, 42 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA,
BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE,
EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP,
KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
KZ, MD; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR,
GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR.
(English). CODEN: PIXXD2. APPLICATION: WO 2003-US30402 20030925.
PRIORITY: US 2002-PV414940 20020930; US 2002-PV421904 20021029; US
2002-PV433834 20021216; US 2003-PV443662 20030130.
GI



I

AB Disclosed are oral pharmaceutical compns., kits and methods of treating and preventing Hepatitis C Viral (HCV) infections wherein Compound (I), a potent inhibitor of HCV serine protease, or a pharmaceutically acceptable salt thereof, is administered in a selected dosage range. Also disclosed are the use of I or a pharmaceutically acceptable salt thereof, as a control substance for validating an HCV replication assay and also as a control substance for determining the relative effectiveness of one or more substances, alone or in combination, to inhibit the replication of HCV.
IT 300832-84-2
RL: PAC (Pharmacological activity); PEP (Physical, engineering or
chemical process); PYP (Physical process); THU (Therapeutic use);
BIOL (Biological study); PROC (Process); USES (Uses)
(potent inhibitor of HCV serine protease)

=> FIL CAPLUS
COST IN U.S. DOLLARS SINCE FILE
TOTAL
ENTRY
SESSION
FULL ESTIMATED COST 5.12
14.95

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE
TOTAL
ENTRY
SESSION
CA SUBSCRIBER PRICE -0.70
0.70

FILE 'CAPLUS' ENTERED AT 14:29:30 ON 26 OCT 2004
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FILE COVERS 1907 - 26 Oct 2004 VOL 141 ISS 18
FILE LAST UPDATED: 25 Oct 2004 (20041025/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S L1/PUR
15 L1
201134 PUR/RL
L7 0 L1/PUR
(L1 (L) PUR/RL)

=> FIL CAPLUS
COST IN U.S. DOLLARS SINCE FILE
TOTAL
ENTRY
SESSION
FULL ESTIMATED COST 2.26
17.21

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE
TOTAL
ENTRY
SESSION

CA SUBSCRIBER PRICE 0.00 -
0.70

FILE 'CAPLUS' ENTERED AT 14:29:48 ON 26 OCT 2004
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FILE COVERS 1907 - 26 Oct 2004 VOL 141 ISS 18
FILE LAST UPDATED: 25 Oct 2004 (20041025/ED)

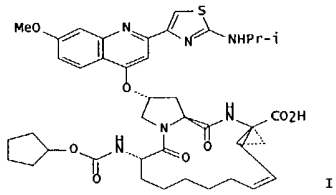
This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S (L1/SPN OR L1/CPN)
15 L1
1660968 SPN/RL
6 L1/SPN
(L1 (L) SPN/RL)
15 L1
1155 CPN/RL
0 L1/CPN
(L1 (L) CPN/RL)
L8 6 (L1/SPN OR L1/CPN)

=> FOCUS L8
PROCESSING COMPLETED FOR L8
L9 6 FOCUS L8 1-

=> DIS L9 1- CBIB ABS HITRN
YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):Y

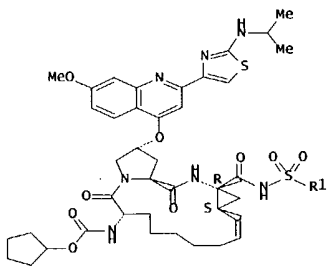
L9 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
2004:580783 Document No. 141:261053 Synthesis of BILN 2061, an HCV NS3
Protease Inhibitor with Proven Antiviral Effect in Humans.
Faucher,
Anne-Marie; Bailey, Murray D.; Beaulieu, Pierre L.; Brochu, Christian;
Duceppe, Jean-Simon; Ferland, Jean-Marie; Ghiro, Elise; Gorys, Vida;
Halmos, Ted; Kawai, Stephen H.; Poirier, Martin; Simoneau, Bruno;
Tsantrizos, Youla S.; Llinas-Brunet, Montse (Chemistry Department,
Boehringer Ingelheim (Canada) Ltd., Laval, QC, H7S 2G5, Can.). Organic
Letters, 6(17), 2901-2904 (English) 2004. CODEN: ORLEF7. ISSN: 1523-7060. Publisher: American Chemical Society.
GI



I

AB The synthesis of BILN 2061 (I), a hepatitis C virus (HCV) NS3 protease inhibitor with proven antiviral effect in humans, was accomplished in a convergent manner from four building blocks. The procedure described here was suitable for the preparation of multigram quantities of BILN 2061 for preclin. pharmacol. evaluation.
IT 300832-84-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(preparation of peptidyl macrocycle BILN-2061, an HCV NS3 protease inhibitor
with proven antiviral effect in humans)

L9 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
2004:370958 Document No. 140:357673 Preparation of macrocyclic peptides
active against the hepatitis C virus. Llinas-Brunet, Montse; Bailey,
Murray D. (Boehringer Ingelheim International G.m.b.h., Germany). PCT
Int. Appl. WO 2004037855 A1 20040506, 40 pp. DESIGNATED STATES: W: AE,
AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID,
IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD,
SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD; RW: AT, BE, BF, BJ, CF, CG, CH, CI,
CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL,
PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2.
APPLICATION: WO
2003-CA1604 20031020. PRIORITY: US 2002-PV421414 20021025; US 2002-PV433820 20021216; US 2003-PV442768 20030127.
GI

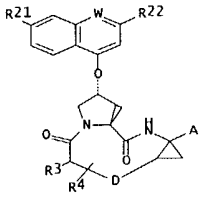


I

AB Macrocyclic peptides I [R1 is (un)substituted alkyl, cycloalkyl, alkylcycloalkyl, aryl or heteroaryl] or their pharmaceutically-acceptable salts were prepared as inhibitors of the hepatitis C virus (HCV) NS3 protease. Thus, I (R = Me) was prepared by a multistep sequence involving peptide coupling, olefin metathesis to form the macrocycle and methanesulfonamidation.
IT 300832-84-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of macrocyclic peptides active against the hepatitis C virus)

L9 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
2004:168624 Document No. 140:350045 Structure-activity study on a novel
series of macrocyclic inhibitors of the hepatitis C virus NS3 protease
leading to the discovery of BILN 2061. Llinas-Brunet, Montse; Bailey,
Murray D.; Bolger, Gordon; Brochu, Christian; Faucher, Anne-Marie;
Ferland, Jean Marie; Garneau, Michel; Ghiro, Elise; Gorys, Vida;
Grand-Maitre, Chantal; Halmos, Ted; Lapeyre-Paquette, Nicole; Liard,
Francine; Poirier, Martin; Rheaume, Manon; Tsantrizos, Youla S.; Lamarre,
Daniel (Departments of Chemistry and Biological Sciences, Boehringer
Ingelheim (Canada) Ltd., Laval, QC, H7S 2G5, Can.). Journal of Medicinal
Chemistry, 47(7), 1605-1608 (English) 2004. CODEN: JMCMAR. ISSN:
0022-2623. Publisher: American Chemical Society.
AB From the discovery of competitive hexapeptide inhibitors, potent and selective HCV NS3 protease macrocyclic inhibitors have been identified. Structure-activity relationship studies were performed focusing on optimizing the N-terminal carbamate and the aromatic substituent on the (4R)-hydroxyproline moiety. Inhibitors meeting the potency criteria in the cell-based assay and with improved oral bioavailability in rats were identified. BILN 2061 was selected as the best compound, the first NS3 protease inhibitor reported with antiviral activity in man.
IT 300832-84-2P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic
preparation); BIOL (Biological study); PREP (Preparation)
(BILN 2061; structure-activity study on a novel series of macrocyclic
inhibitors of the hepatitis C virus NS3 protease leading to the
discovery of BILN 2061)

L9 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
2003:648255 Document No. 139:197768 Preparation of macrocyclic peptides
active against the hepatitis C virus. Tsantrizos, Youla S.; Cameron, Dale
R.; Faucher, Anne-Marie; Ghiro, Elise; Goudreau, Nathalie; Halmos, Teddy;
Llinas-Brunet, Montse (Boehringer Ingelheim (Canada) Ltd., Can.). U.S. US
6608027 B1 20030819, 90 pp., Cont.-in-part of U.S. Ser. No. 542,675,
abandoned. (English). CODEN: USXXAM. APPLICATION: US 2001-760946
20010116. PRIORITY: US 1999-PV128011 19990406; US 2000-542675 20000403.
GI



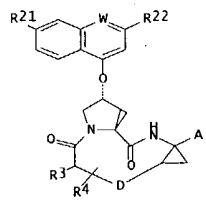
I

AB Macrocyclic peptides I [W = CH or N; R21 = H, halo, alkyl, cycloalkyl, haloalkyl, alkoxy, cycloalkoxy, hydroxy, or an amino group; R22 = H, halo, alkyl, cycloalkyl, haloalkyl, thioalkyl, alkoxy, cycloalkoxy, alkoxyalkyl, cycloalkyl, aryl or heteroaryl; R3 = hydroxy, NH2, aryl- or heteroarylamino, NHCOR32, CONHR32, CO2R32, where R32 is alkyl or cycloalkyl; D is a 5 to 10-atom saturated or unsatd. alkylene chain optionally containing one to three heteroatoms independently selected from: O, S, or NH or substituted imino; R4 = H or from one to three substituents at any carbon atom of chain D; A is an amide or carboxylic acid group or a pharmaceutically acceptable salt or ester; two diastereomers may exist at the cyclopropane moiety] were prepared which are active in-vitro and in cellular assays against the NS3 protease of the hepatitis C virus. Thus, macrocyclic peptide I [W = N; R21, R22, R4 = H; A = CO2H; R3CH-D = (S)-(Me3CO2CNH)CH(CH2)3CH:CH(CH2)2-E (syn to acid)] was prepared and showed IC50 > 0.1 μM in the full-length NS3-NS4A heterodimer protein fluorogenic assay.

IT 300832-84-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(preparation of macrocyclic peptides active against the hepatitis C virus)

L9 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
2003:511084 Document No. 139:69527 Preparation of macrocyclic compounds as
inhibitors of hepatitis C virus. Campbell, Jeffrey Allen; Good, Andrew
Charles (Bristol-Myers Squibb Company, USA). PCT Int. Appl. WO 2003053349
A2 20030703, 225 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ,
BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC,
EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP,
KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO,
NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM;
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR,
IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN:
PIXXD2. APPLICATION: WO 2000-CA353 20000403. PRIORITY: US 1999-PV128011
19990406.

GI



I

AB Macrocyclic peptides I [W = CH or N; R21 = H, halo, alkyl, cycloalkyl, haloalkyl, alkoxy, cycloalkoxy, hydroxy, or an amino group; R22 = H, halo, alkyl, cycloalkyl, haloalkyl, thioalkyl, alkoxy, cycloalkoxy, alkoxyalkyl, cycloalkyl, aryl or heteroaryl; R3 = hydroxy, NH2, aryl- or heteroarylamino, NHCOR32, CONHR32, CO2R32, where R32 is alkyl or cycloalkyl; D is a 5 to 10-atom saturated or unsatd. alkylene chain optionally containing one to three heteroatoms independently selected from: O, S, or NH or substituted imino; R4 = H or from one to three substituents at any carbon atom of chain D; A is an amide or carboxylic acid group or a pharmaceutically acceptable salt or ester; two diastereomers may exist at the cyclopropane moiety] were prepared which are active in-vitro and in cellular assays against the NS3 protease of the hepatitis C virus . Thus, macrocyclic peptide I [W = N; R21, R22, R4 = H; A = CO2H; R3CH-D = (S)-(Me3CO2CNH)CH(CH2)3CH:CH(CH2)2-E (syn to acid)] was prepared and showed IC50 > 0.1 μM in the full-length NS3-NS4A heterodimer protein fluorogenic assay.

IT 300832-84-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(preparation of macrocyclic peptides active against the hepatitis C virus)

=> FIL REGISTRY
COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY
SESSION
FULL ESTIMATED COST 25.57 42.78

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL
ENTRY
SESSION
CA SUBSCRIBER PRICE -4.20 4.90

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STRUCTURE FILE UPDATES: 25 OCT 2004 HIGHEST RN 769101-30-6
DICTIONARY FILE UPDATES: 25 OCT 2004 HIGHEST RN 769101-30-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d his

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GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR.
(English). CODEN: PIXXD2. APPLICATION: WO 2002-US39926 20021213.
PRIORITY: US 2001-PV344080 20011220; US 2002-PV382103 20020520.

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to macrocyclic compds. I [R1 = (cyclo)alkyl; R2 = H, halo, alkyl, alkoxy, cycloalkoxy, (un)substituted aryl or heterocyclyl; R3 = H, halo, CF3, alkoxy, cycloalkoxy; R4 = NH2 or NHR6, where R6 is alkanoyl, alkylaminocarbonyl, or carbalkoxy; Q is a 3-9 atom (un)saturated alkylene chain optionally containing 1-3 heteroatoms O, S, SO, or SO2], including methods for their synthesis and use in pharmaceutical compns. for therapeutic or prophylactic prevention or treatment of hepatitis C virus (HCV) infection. Thus, 3,13-diazatricyclo[11.3.0.04,6]hexadec-7-ene derivative II was prepared by a multistep procedure and assayed for inhibition of HCV NS3/4A protease (IC50 < 5 μM).

IT 300832-84-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of macrocyclic compds. as inhibitors of hepatitis C virus)

L9 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
2000:725652 Document No. 133:296659 Preparation of macrocyclic peptides
active against the hepatitis C virus. Tsantrizos, Youla S.; Cameron, Dale
R.; Faucher, Anne-marie; Ghiro, Elise; Goudreau, Nathalie; Halmos, Teddy;
Llinas-brunet, Montse (Boehringer Ingelheim (Canada) Ltd., Can.). PCT
Int. Appl. WO 2000059929 A1 20001012, 154 pp. DESIGNATED STATES: W: AE,
AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE,
DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 26 Oct 2004  VOL 141 ISS 18
FILE LAST UPDATED: 25 Oct 2004  (20041025/ED)

 This file contains CAS Registry Numbers for easy and accurate
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ACCESSION NUMBER:        2004:252197  HCAPLUS Full-text
DOCUMENT NUMBER:         140:281350
TITLE:                   Spiro compounds for inhibiting the first-
pass effect
INVENTOR(S):             Harris, James W.
PATENT ASSIGNEE(S):      Bioavailability System, LLC, USA
SOURCE:                  U.S. Pat. Appl. Publ., 133 pp., Cont.-in-
part of U.S.
                         Ser. No. 793,416.
                         CODEN: USXXCO
DOCUMENT TYPE:           Patent
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FAMILY ACC. NUM. COUNT:  5
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     US 6248776           B1    20010619    US 1999-251467
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OTHER SOURCE(S):         MARPAT 140:281350

L14  ANSWER 2 OF 3  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:        2003:886572  HCAPLUS Full-text
DOCUMENT NUMBER:         140:122161
TITLE:                   An NS3 protease inhibitor with antiviral
effects in
                         humans infected with hepatitis C virus
AUTHOR(S):               Lamarre, Daniel; Anderson, Paul C.; Bailey,
Murray;
                         Beaulieu, Pierre; Bolger, Gordon; Bonneau,
Pierre;
                         Boes, Michael; Cameron, Dale R.; Cartier,
Mireille;
                         Cordingley, Michael G.; Faucher, Anne-Marie;
Goudreau,
                         Nathalie; Kawai, Stephen H.; Kukolj, George;
Lagace,
                         Lisette; LaPlante, Steven R.; Narjes, Hans;
Poupart,
                         Marc-Andre; Rancourt, Jean; Sentjens, Roel
E.; St.
                         George, Roger; Simoneau, Bruno; Steinmann,
Gerhard;
                         Thibeault, Diane; Tsantrizos, Youla S.;
Weldon, Steven
                         M.; Yong, Chan-Loi; Llinas-Brunet, Montse
CORPORATE SOURCE:        Departments of Biological Sciences,
Boehringer
                         Ingelheim (Canada) Ltd, Laval, QC, H7S 2G5,
Can.
SOURCE:                  Nature (London, United Kingdom) (2003),
                         426(6963), 186-189
                         CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER:               Nature Publishing Group
DOCUMENT TYPE:           Journal
LANGUAGE:                English
REFERENCE COUNT:         30    THERE ARE 30 CITED REFERENCES
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L14  ANSWER 3 OF 3  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:        2000:725652  HCAPLUS Full-text
DOCUMENT NUMBER:         133:296659
TITLE:                   Preparation of macrocyclic peptides active
against the
                         hepatitis C virus
INVENTOR(S):             Tsantrizos, Youla S.; Cameron, Dale R.;
Faucher,
                         Anne-marie; Ghiro, Elise; Goudreau,
Nathalie; Halmos,
                         Teddy; Llinas-brunet, Montse
PATENT ASSIGNEE(S):      Boehringer Ingelheim (Canada) Ltd., Can.
SOURCE:                  PCT Int. Appl., 154 pp.
                         CODEN: PIXXD2
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OTHER SOURCE(S):           MARPAT 133:296659
REFERENCE COUNT:           1       THERE ARE 1 CITED REFERENCES AVAILABLE
FOR THIS
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RE FORMAT


=> d l14 1 hitstr

L14  ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2004 ACS on STN
IT   300832-84-2, BILN 2061
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
       (spiro compds. for inhibiting the first-pass effect)
RN   300832-84-2  HCAPLUS
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carboxylic
     acid, 6-[[(cyclopentyloxy)carbonyl]amino]-
1,2,3,6,7,8,9,10,11,13a,14,15,16
     ,16a-tetradecahydro-2-[[7-methoxy-2-[2-[(1-methylethyl)amino]-4-
thiazolyl]-
     4-quinolinyl]oxy]-5,16-dioxo-, (2R,6S,12Z,13aS,14aR,16aS)- (9CI)
(CA
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Absolute stereochemistry.
Double bond geometry as shown.
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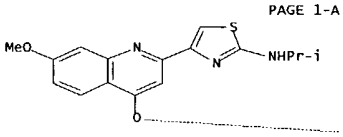
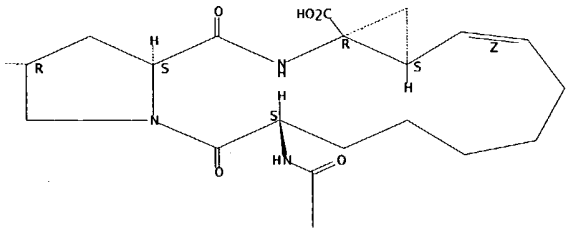


PAGE 1-B



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       ALUMINIUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE,
BABS,
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BIOTECHABS,
       BIOTECHDS, BIOTECHNO, BLLDB, CABA, CANCERLIT, ...'
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143 FILES IN THE FILE LIST IN STNINDEX

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L15  QUE BILN 2061

=> d rank
F1          42   EMBASE
F2          22   SCISEARCH
F3          18   BIOSIS
F4          15   INVESTEXT
F5          13   MEDLINE
F6          11   PCTFULL
F7          10   CAPLUS
F8          10   DDFU
F9          10   DRUGU
F10          8   BIOTECHNO
F11          6   USPATFULL
F12          4   LIFESCI
F13          4   PASCAL
F14          4   TOXCENTER
F15          3   ESBIOBASE
F16          3   IMSDRUGNEWS
F17          3   NLDB
F18          2   ADISCTI
F19          2   BIOENG
F20          2   CBNB
F21          2   COMPENDEX
F22          2   PHIN
F23          2   WPIDS
F24          2   WPINDEX
F25          1   BABS
F26          1   CIN
F27          1   EMBAL
F28          1   IFIPAT
F29          1   PROMT
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=> index f1-f29
COST IN U.S. DOLLARS                        SINCE FILE
TOTAL
                                               ENTRY
SESSION
FULL ESTIMATED COST                             1.14
94.22

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)  SINCE FILE
TOTAL
                                               ENTRY
SESSION
CA SUBSCRIBER PRICE                             0.00
4.90

INDEX 'EMBASE, SCISEARCH, BIOSIS, INVESTEXT, MEDLINE, PCTFULL,
CAPLUS, DDFU,
      DRUGU, BIOTECHNO, USPATFULL, LIFESCI, PASCAL, TOXCENTER,
ESBIOBASE,
      IMSDRUGNEWS, NLDB, ADISCTI, BIOENG, CBNB, COMPENDEX, PHIN,
WPIDS,
      WPINDEX, BABS, CIN, EMBAL, IFIPAT, PROMT' ENTERED AT 15:26:20
ON 26 OCT 2004

29 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> d his l14-

     (FILE 'HCAPLUS' ENTERED AT 14:32:46 ON 26 OCT 2004)
L14            3 L10 AND PD<20030327

     FILE 'HOME' ENTERED AT 14:39:45 ON 26 OCT 2004

     INDEX '1MOBILITY, 2MOBILITY, ABI-INFORM, ADISCTI, AEROSPACE,
AGRICOLA,
     ALUMINIUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE,
BABS,
     BIBLIODATA, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS,
BIOTECHABS,
     BIOTECHDS, BIOTECHNO, BLLDB, CABA, CANCERLIT, ...' ENTERED AT
15:24:55 ON
     26 OCT 2004
                SEA BILN 2061
                ---------
               2   FILE ADISCTI
               1   FILE BABS
               2   FILE BIOENG
              18   FILE BIOSIS
               8   FILE BIOTECHNO
              10   FILE CAPLUS
               2   FILE CBNB
               1   FILE CIN
               2   FILE COMPENDEX
              10   FILE DDFU
              10   FILE DRUGU
               1   FILE EMBAL
              42   FILE EMBASE
               3   FILE ESBIOBASE
               1   FILE IFIPAT
               3   FILE IMSDRUGNEWS
              15   FILE INVESTEXT
               4   FILE LIFESCI
              13   FILE MEDLINE
               3   FILE NLDB
               4   FILE PASCAL
              11   FILE PCTFULL
               2   FILE PHIN
               1   FILE PROMT
              22   FILE SCISEARCH
               4   FILE TOXCENTER
               6   FILE USPATFULL
               2   FILE WPIDS
               2   FILE WPINDEX
L15             QUE BILN 2061
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     INDEX 'EMBASE, SCISEARCH, BIOSIS, INVESTEXT, MEDLINE, PCTFULL,
CAPLUS,
     DDFU, DRUGU, BIOTECHNO, USPATFULL, LIFESCI, PASCAL, TOXCENTER,
ESBIOBASE,
     IMSDRUGNEWS, NLDB, ADISCTI, BIOENG, CBNB, COMPENDEX, PHIN,
WPIDS,
     WPINDEX, BABS, CIN, EMBAL, IFIPAT, PROMT' ENTERED AT 15:26:20 ON
26 OCT
     2004

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L16  QUE L15 AND CRYSTAL?

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F2            6   USPATFULL
F3            4   EMBASE
F4            3   SCISEARCH
F5            3   BIOTECHNO


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TOTAL
                                                  ENTRY
SESSION
FULL ESTIMATED COST                                1.71
95.93

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE
TOTAL
                                                  ENTRY
SESSION
CA SUBSCRIBER PRICE                                0.00
4.90

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=> l16, dup rem
L17           0 L16, DUP REM
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=> l16
L18          25 L16

=> dup rem
ENTER L# LIST OR (END):l18
PROCESSING COMPLETED FOR L18
L19          21 DUP REM L18 (4 DUPLICATES REMOVED)

=> l19 and pd<20030327
   1 FILES SEARCHED...
   3 FILES SEARCHED...
L20           2 L19 AND PD<20030327

=> d l20 1-2 ibib hitstr abs kwic
'HITSTR' IS NOT A VALID FORMAT FOR FILE 'EMBASE'

The following are valid formats:

The default display format is BIB.

ABS --------- AB
ALL --------- AN, DN, TI, AU, CS, SO, PUI, CY, DT, FS, LA, SL, AB,
              CT, RN, CN, NP, CO, GEN
BIB --------- AN, DN, TI, AU, CS, SO, PUI, CY, DT, FS, LA, SL
CBIB -------- Compressed bibliographic data
DALL -------- ALL, delimited for post-processing
IABS -------- ABS, with a text label
IALL -------- ALL, indented with text labels
IBIB -------- BIB, indented with text labels
IND --------- CT, RN, CN, NP, CO, GEN
TRIAL ------  TI, CT, RN, CN, NP, CO, GEN
 (SAM, TRI)
HIT --------- All fields containing hit terms
HITIND ------ IND
KWIC -------- All hit terms plus 20 words on either side
OCC --------- List of display fields containing hit terms
              and number of occurrences in each field

Hit terms will be highlighted in all displayable fields.

To display a particular field or fields,  enter the display field
codes.  For a list of display field codes, enter 'HELP DFIELDS'
at an arrow prompt (=>).  Examples of formats include: 'BIB';
'AB'; 'SO,ST'.  You may specify the format fields in any order,
and the information will be displayed in the same order as the
format specification.

The same formats (except for HIT, HITIND, KWIC, and OCC) may be
used with the DISPLAY ACC command to display the record for a
specified Accession Number.

ENTER DISPLAY FORMAT (BIB):iall

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     on STN

ACCESSION NUMBER:    2003468113  EMBASE  Full-text
TITLE:               Current therapy and new molecular approaches to
antiviral
                     treatment and prevention of hepatitis C.
AUTHOR:              Hugle T.; Cerny A.
CORPORATE SOURCE:    Dr. A. Cerny, Clinica Medica, Ospedale Civico,
CH-6903
                     Lugano, Switzerland. andreas.cerny@bluewin.ch
SOURCE:              Reviews in Medical Virology, (2003) 13/6
                     (361-371).
                     Refs: 79
                     ISSN: 1052-9276  CODEN: RMVIEW
COUNTRY:             United Kingdom
DOCUMENT TYPE:       Journal; General Review
FILE SEGMENT:        004     Microbiology
                     030     Pharmacology
                     037     Drug Literature Index
                     038     Adverse Reactions Titles
                     039     Pharmacy
LANGUAGE:            English
SUMMARY LANGUAGE:    English
ABSTRACT:
Current therapeutic options for hepatitis C are limited, especially
for
genotype 1. For genotypes 2 and 3, pegylated interferon in
combination with
ribavirin, can lead to a sustained virological response in up to 80%
of
patients. Unfortunately, adverse effects of IFN and ribavirin are a
major
problem and the list of contraindications for HCV therapy is long,
including
decompensated cirrhosis of the liver and psychiatric disorders.
Therefore,
alternative therapeutic approaches are needed. New delivery options
for IFN and
ribavirin are aimed at optimising efficiency and reducing adverse
effects.
Recent progress in the molecular virology of HCV has identified new
targets for
antiviral intervention. Inhibition of HCV gene expression and
replication as
well as immunotherapeutic concepts aimed at enhancing the cellular
immune
response against HCV are being explored. Solution of the crystal
structures of HCV key enzymes led to the design of specific
inhibitors
including compounds active against the well characterised NS3 serine
protease
and RNA-dependent RNA polymerase which are currently in the early
phase
clinical investigation. New strategies for inhibiting HCV gene
expression
include the use of antisense oligodeoxynucleotides and ribozymes.
Immunomodulation by agents such as inosine monophosphate
dehydrogenase
inhibitors, thymosin-alpha 1, histamine or amantadine are being
```

studied in
combination with IFN and/or ribavirin. Immunotherapeutic vaccination
with
recombinant HCV E1 protein improved host immunity against HCV and
thus seems to
be a promising new option. Copyright .COPYRGT. 2003 John Wiley &
Sons, Ltd.

CONTROLLED TERM: Medical Descriptors:
*hepatitis C: DT, drug therapy
*hepatitis C: ET, etiology
*hepatitis C: PC, prevention
*infection prevention
virus gene
genotype
drug response
drug contraindication
drug delivery system
side effect: SI, side effect
gene expression
drug targeting
immunotherapy
enzyme structure
crystal structure
drug design
drug activity
antiviral activity
protein targeting
immunomodulation
vaccination
Hepatitis C virus
immune response
cellular immunity
hemolytic anemia: SI, side effect
mental disease: SI, side effect
flu like syndrome: SI, side effect
leukopenia: SI, side effect
thrombocytopenia: SI, side effect
teratogenicity
virus replication
drug hypersensitivity: SI, side effect
rash: SI, side effect
human
nonhuman
clinical trial
review
Drug Descriptors:
alpha interferon: AE, adverse drug reaction
alpha interferon: CT, clinical trial
alpha interferon: CB, drug combination
alpha interferon: DT, drug therapy
alpha interferon: TO, drug toxicity
alpha interferon: PR, pharmaceutics
alpha interferon: PD, pharmacology
alpha interferon: SC, subcutaneous drug
administration
ribavirin: AE, adverse drug reaction
ribavirin: CT, clinical trial
ribavirin: CB, drug combination
ribavirin: CM, drug comparison
ribavirin: DT, drug therapy
ribavirin: PK, pharmacokinetics
ribavirin: PD, pharmacology
ribavirin: PO, oral drug administration
albumin conjugate: PR, pharmaceutics
liposome: PR, pharmaceutics
polyaminoacid: PR, pharmaceutics
polyaminoacid: PO, oral drug administration
ribavirin derivative: AE, adverse drug reaction
ribavirin derivative: CT, clinical trial
ribavirin derivative: CB, drug combination
ribavirin derivative: CM, drug comparison
ribavirin derivative: DT, drug therapy
ribavirin derivative: PD, pharmacology
viramidine: AE, adverse drug reaction
viramidine: CT, clinical trial
viramidine: CB, drug combination
viramidine: CM, drug comparison
viramidine: DT, drug therapy
viramidine: PD, pharmacology
levovirin: AE, adverse drug reaction
levovirin: CT, clinical trial
levovirin: CM, drug comparison
levovirin: DT, drug therapy
levovirin: PD, pharmacology
proteinase inhibitor: AE, adverse drug reaction
proteinase inhibitor: CT, clinical trial
proteinase inhibitor: DO, drug dose
proteinase inhibitor: DT, drug therapy
proteinase inhibitor: PK, pharmacokinetics
proteinase inhibitor: PD, pharmacology
proteinase inhibitor: PO, oral drug
administration
biln 2061: AE, adverse drug reaction
biln 2061: CT, clinical trial
biln 2061: DO, drug dose
biln 2061: DT, drug therapy
biln 2061: PK, pharmacokinetics
biln 2061: PD, pharmacology
biln 2061: PO, oral drug administration
vx 950: DT, drug therapy
vx 950: PD, pharmacology
virus protein
protein NS5B
RNA directed DNA polymerase inhibitor: CT,
clinical trial
RNA directed DNA polymerase inhibitor: DT, drug
therapy
RNA directed DNA polymerase inhibitor: PD,
pharmacology
jtk 003: CT, clinical trial
jtk 003: DT, drug therapy
jtk 003: PD, pharmacology
ribozyme: AE, adverse drug reaction
ribozyme: CT, clinical trial
ribozyme: DT, drug therapy
ribozyme: TO, drug toxicity
ribozyme: PD, pharmacology
hepatozyme: AE, adverse drug reaction
hepatozyme: CT, clinical trial
hepatozyme: DT, drug therapy
hepatozyme: TO, drug toxicity
hepatozyme: PD, pharmacology
antisense oligodeoxynucleotide: CT, clinical
trial
antisense oligodeoxynucleotide: DT, drug therapy
antisense oligodeoxynucleotide: PD, pharmacology
isis 14803: CT, clinical trial
isis 14803: DT, drug therapy
isis 14803: PD, pharmacology
RNA derivative: DV, drug development
RNA derivative: DT, drug therapy
RNA derivative: PD, pharmacology
small interfering rna: DV, drug development
small interfering rna: DT, drug therapy
small interfering rna: PD, pharmacology
monoclonal antibody: DT, drug therapy
monoclonal antibody: PD, pharmacology
xtl 002: DT, drug therapy
xtl 002: PD, pharmacology
cicavir: DT, drug therapy
cicavir: PD, pharmacology
immunomodulating agent: CB, drug combination
immunomodulating agent: DT, drug therapy
thymosin alpha1: CT, clinical trial
thymosin alpha1: CB, drug combination
thymosin alpha1: DO, drug dose
thymosin alpha1: DT, drug therapy
thymosin alpha1: PD, pharmacology
inosinate dehydrogenase inhibitor: CB, drug
combination
inosinate dehydrogenase inhibitor: DT, drug
therapy
inosinate dehydrogenase inhibitor: PD,
pharmacology
merimepodib: CT, clinical trial
merimepodib: CB, drug combination
merimepodib: DT, drug therapy
merimepodib: PD, pharmacology
unindexed drug
unclassified drug
CAS REGISTRY NO.: (ribavirin) 36791-04-5; (proteinase inhibitor)
37205-61-1;
(thymosin alpha1) 69521-94-4; (merimepodib)
198821-22-6,
198821-38-4
CHEMICAL NAME: (1) Vx 950; (2) Jtk 003; Biln 2061; Isis 14803;
Xtl 002
COMPANY NAME: (1) Vertex; (2) Akros; Ribozyme Pharmaceuticals;
NABI;
Sciclone; RegeneRx; Maxim

L20 ANSWER 2 OF 2 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS
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on STN
ACCESSION NUMBER: 2003195244 EMBASE Full-text
TITLE: Hepatitis C virus therapies: Current treatments,
targets
and future perspectives.
AUTHOR: Walker M.P.; Appleby T.C.; Zhong W.; Lau J.Y.N.;
Hong Z.
CORPORATE SOURCE: Z. Hong, Ribapharm Inc., Hyland Avenue, Costa
Mesa, CA,
United States. zhihong@ribapharm.com
SOURCE: Antiviral Chemistry and Chemotherapy, (2003) 14/1
(1-21).
Refs: 208
ISSN: 0956-3202 CODEN: ACCHEH
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Chronic hepatitis C virus (HCV) infection is the cause of an emerging
global
epidemic of chronic liver disease. Current combination therapies are
at best
80% efficacious and are often poorly tolerated. Strategies to improve
the
therapeutic response include the development of novel interferons,
nucleoside
analogues with reduced haemolysis compared with ribavirin and inosine
5'-monophosphate dehydrogenase inhibitors. Compounds in preclinical
or early
clinical trials include small molecules that inhibit virus-specific
enzymes
(such as the serine proteases, RNA polymerase and helicase) or
interfere with
translation (including antisense molecules, iRNA and ribozymes).
Advances in
understanding HCV replication, obtaining a sub-genomic replicon and
contriving
potential small animal models, in addition to solving
crystallographic
structures for the replication enzymes, have improved prospects for
developing
novel therapies. This review summarizes current and evolving
treatments for
chronic hepatitis C infection. In addition, progress in HCV targets
and drug
discovery tools valuable in the search for novel anti-HCV agents is
detailed.

CONTROLLED TERM:

Medical Descriptors:
*hepatitis C: DT, drug therapy
*hepatitis C: EP, epidemiology
*hepatitis C: ET, etiology
*chronic liver disease: ET, etiology
drug efficacy
drug tolerance
hemolytic anemia: SI, side effect
side effect: SI, side effect
alanine aminotransferase blood level
virus replication
replicon
crystal structure
RNA translation
untranslated region
internal ribosome entry site
monotherapy
virus load
treatment outcome
treatment indication
immunomodulation
drug safety
treatment failure
chimpanzee
transgenic mouse
Hepatitis GB virus B
IC 50
structure activity relation
drug structure
virus assembly
human
nonhuman
clinical trial
review
priority journal
Drug Descriptors:
*antivirus agent: AE, adverse drug reaction
*antivirus agent: CT, clinical trial
*antivirus agent: AN, drug analysis
*antivirus agent: CB, drug combination
*antivirus agent: CM, drug comparison
*antivirus agent: DV, drug development
*antivirus agent: DO, drug dose
*antivirus agent: DT, drug therapy
*antivirus agent: PD, pharmacology
*antivirus agent: IV, intravenous drug
administration
*antivirus agent: SC, subcutaneous drug
administration
alpha interferon: AE, adverse drug reaction
alpha interferon: CB, drug combination
alpha interferon: CM, drug comparison
alpha interferon: DO, drug dose
alpha interferon: DT, drug therapy
alpha interferon: PD, pharmacology
nucleoside derivative: AN, drug analysis
nucleoside derivative: CM, drug comparison
comparison
therapy
pharmacology
comparison
drug
administration
comparison
drug
administration
administration
nucleoside derivative: DV, drug development
nucleoside derivative: PR, pharmaceutics
nucleoside derivative: PD, pharmacology
ribavirin: AE, adverse drug reaction
ribavirin: CT, clinical trial
ribavirin: CB, drug combination
ribavirin: CM, drug comparison
ribavirin: DO, drug dose
ribavirin: DT, drug therapy
ribavirin: PD, pharmacology
inosinate dehydrogenase inhibitor: CM, drug
inosinate dehydrogenase inhibitor: DT, drug
inosinate dehydrogenase inhibitor: PD,
serine proteinase: EC, endogenous compound
RNA polymerase: EC, endogenous compound
helicase: EC, endogenous compound
ribozyme: EC, endogenous compound
recombinant alpha2a interferon: CM, drug
recombinant alpha2a interferon: DO, drug dose
recombinant alpha2a interferon: DT, drug therapy
recombinant alpha2a interferon: PD, pharmacology
recombinant alpha2a interferon: SC, subcutaneous
administration
recombinant alpha2b interferon: CM, drug
recombinant alpha2b interferon: DO, drug dose
recombinant alpha2b interferon: DT, drug therapy
recombinant alpha2b interferon: PD, pharmacology
recombinant alpha2b interferon: SC, subcutaneous
administration
consensus interferon: CM, drug comparison
consensus interferon: DO, drug dose
consensus interferon: DT, drug therapy
consensus interferon: PD, pharmacology
consensus interferon: SC, subcutaneous drug
administration
peginterferon alpha2b: CT, clinical trial
peginterferon alpha2b: CB, drug combination
peginterferon alpha2b: CM, drug comparison
peginterferon alpha2b: DO, drug dose
peginterferon alpha2b: DT, drug therapy
peginterferon alpha2b: PD, pharmacology
peginterferon alpha2a: CT, clinical trial
peginterferon alpha2a: CB, drug combination
peginterferon alpha2a: CM, drug comparison
peginterferon alpha2a: DO, drug dose
peginterferon alpha2a: DT, drug therapy
peginterferon alpha2a: PD, pharmacology
levovirin: CT, clinical trial
levovirin: AN, drug analysis
levovirin: CM, drug comparison
levovirin: DV, drug development
levovirin: DO, drug dose
levovirin: DT, drug therapy
levovirin: PD, pharmacology
viramidine: CT, clinical trial
viramidine: AN, drug analysis
viramidine: CM, drug comparison
viramidine: DV, drug development
viramidine: DO, drug dose
viramidine: DT, drug therapy
viramidine: PD, pharmacology
merimepodib: CT, clinical trial
merimepodib: AN, drug analysis
merimepodib: CB, drug combination
merimepodib: CM, drug comparison
merimepodib: DV, drug development
merimepodib: DT, drug therapy
merimepodib: PD, pharmacology
thymosin alpha1: CT, clinical trial
thymosin alpha1: AN, drug analysis
thymosin alpha1: CB, drug combination
thymosin alpha1: DV, drug development
thymosin alpha1: DO, drug dose
thymosin alpha1: DT, drug therapy
thymosin alpha1: PD, pharmacology
thymosin alpha1: SC, subcutaneous drug
administration
amantadine: CT, clinical trial
amantadine: AN, drug analysis
amantadine: CB, drug combination
amantadine: CM, drug comparison
amantadine: DV, drug development
amantadine: PD, pharmacology
recombinant interleukin 12: CT, clinical trial
recombinant interleukin 12: AN, drug analysis
recombinant interleukin 12: CB, drug combination
recombinant interleukin 12: CM, drug comparison
recombinant interleukin 12: DV, drug development
recombinant interleukin 12: DO, drug dose
recombinant interleukin 12: DT, drug therapy
recombinant interleukin 12: PD, pharmacology
histamine: CT, clinical trial
histamine: AN, drug analysis
histamine: CB, drug combination
histamine: DV, drug development
histamine: DT, drug therapy
histamine: PD, pharmacology
gamma interferon: CT, clinical trial
gamma interferon: AN, drug analysis
gamma interferon: CB, drug combination
gamma interferon: DV, drug development
gamma interferon: DT, drug therapy
gamma interferon: PD, pharmacology
proteinase inhibitor: CT, clinical trial
proteinase inhibitor: DO, drug dose
proteinase inhibitor: PD, pharmacology
proteinase inhibitor: PO, oral drug
administration
biln 2061: CT, clinical trial
biln 2061: DO, drug dose
biln 2061: PD, pharmacology
biln 2061: PO, oral drug administration
peptide derivative: AN, drug analysis
peptide derivative: DV, drug development
peptide derivative: PD, pharmacology
peptide alpha keto acid: AN, drug analysis
peptide alpha keto acid: DV, drug development
peptide alpha keto acid: PD, pharmacology
pyrrolidine derivative: AN, drug analysis
pyrrolidine derivative: DV, drug development
pyrrolidine derivative: PD, pharmacology
pyrrolidine 5,5 lactam: AN, drug analysis
pyrrolidine 5,5 lactam: DV, drug development
pyrrolidine 5,5 lactam: PD, pharmacology
IDdb3: DV, drug development
IDdb3: PD, pharmacology
unindexed drug
unclassified drug
isis 14803
gw 3112
gw 2549
gw 0569
n [4 [[[6,7 dihydro 2 (4 methylphenyl) 5h
benzocyclohepten
8 yl]carbonyl]amino]benzyl] n,n dimethyl 2h
tetrahydropyran
4 aminium chloride
1,1' [1,4 phenylenebis(methylene)]bis(1,4,8,11
tetraazacyclotetradecane)

CAS REGISTRY NO.:
(ribavirin) 36791-04-5; (serine proteinase)
37259-58-8;
(RNA polymerase) 9014-24-8; (helicase) 42613-29-
6;
(recombinant alpha2b interferon) 98530-12-2;
(peginterferon
alpha2b) 215647-85-1; (peginterferon alpha2a)
198153-51-4;
(merimepodib) 198821-22-6, 198821-38-4; (thymosin
alpha1)
69521-94-4; (amantadine) 665-66-7, 768-94-5;
(histamine)
51-45-6, 56-92-8, 93443-21-1; (gamma interferon)
82115-62-6; (proteinase inhibitor) 37205-61-1; (n
[4 [[[6,7
dihydro 2 (4 methylphenyl) 5h benzocyclohepten 8
yl]carbonyl]amino]benzyl] n,n dimethyl 2h
tetrahydropyran 4
aminium chloride) 229005-80-5; (1,1' [1,4
phenylenebis(methylene)]bis(1,4,8,11
tetraazacyclotetradecane)) 155148-31-5

CHEMICAL NAME:
(1) Vx 497; (2) Ceplene; (3) Biln 2061; (4) Isis
14803; Zadaxin; Gw 3112; Gw 2549; Gw 0569; Tak
779; Amd
3100; IDdb3

```
COMPANY NAME:          (1) Vertex (United States); (2) Maxim; (3)
Boehringer
                       Ingelheim; (4) Isis (United States); Ribapharm;
Merck
                       (United States); Glaxo SmithKline (United
Kingdom); Bristol
                       Myers Squibb (United States); Celera (United
States);
                       Viropharma; Japanese tobacco; IRBM


=> d his

     (FILE 'HOME' ENTERED AT 14:24:22 ON 26 OCT 2004)

     INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE,
AQUALINE,
     AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS, BIOTECHABS,
BIOTECHDS,
     BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN,
CONFSCI, CROPB,
     CROPU, DDFB, DDFU, DGENE, DISSABS, ...' ENTERED AT 14:25:23 ON
26 OCT 2004

     FILE 'REGISTRY' ENTERED AT 14:26:32 ON 26 OCT 2004
L1             1 S 300832-84-2/RN
                 SET SMA OFF
                 DEL SEL Y
                 SEL RN
                 SET SMA LOGIN

     INDEX 'BEILSTEIN, GMELIN' ENTERED AT 14:27:43 ON 26 OCT 2004
                 SEA E1 AND OPTICAL?/FA
               ---------
L2               QUE 300832-84-2/BI AND OPTICAL?/FA
               ---------

     FILE 'CAPLUS' ENTERED AT 14:28:02 ON 26 OCT 2004
L3             0 S L1/BMF

     FILE 'CAPLUS' ENTERED AT 14:28:18 ON 26 OCT 2004
L4             0 S L1/BPN

     FILE 'CAPLUS' ENTERED AT 14:28:28 ON 26 OCT 2004
L5             0 S L1/IMF

     FILE 'CAPLUS' ENTERED AT 14:28:41 ON 26 OCT 2004
L6             1 S L1/PEP

     FILE 'CAPLUS' ENTERED AT 14:29:30 ON 26 OCT 2004
L7             0 S L1/PUR

     FILE 'CAPLUS' ENTERED AT 14:29:48 ON 26 OCT 2004
L8             6 S (L1/SPN OR L1/CPN)
L9             6 FOCUS L8 1-

     FILE 'REGISTRY' ENTERED AT 14:31:45 ON 26 OCT 2004
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     FILE 'HCAPLUS' ENTERED AT 14:32:46 ON 26 OCT 2004
L10           15 S L1
L11            0 L10 AND CRYSTAL
L12            0 L10 AND CRYSTAL?
L13            0 L10 AND ALCOHOL
L14            3 L10 AND PD<20030327

     FILE 'HOME' ENTERED AT 14:39:45 ON 26 OCT 2004

     INDEX '1MOBILITY, 2MOBILITY, ABI-INFORM, ADISCTI, AEROSPACE,
AGRICOLA,
     ALUMINIUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE,
BABS,
     BIBLIODATA, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS,
BIOTECHABS,
     BIOTECHDS, BIOTECHNO, BLLDB, CABA, CANCERLIT, ...' ENTERED AT
15:24:55 ON
     26 OCT 2004
                 SEA BILN 2061
               ---------
               2   FILE ADISCTI
               1   FILE BABS
               2   FILE BIOENG
              18   FILE BIOSIS
               8   FILE BIOTECHNO
              10   FILE CAPLUS
               2   FILE CBNB
               1   FILE CIN
               2   FILE COMPENDEX
              10   FILE DDFU
              10   FILE DRUGU
               1   FILE EMBAL
              42   FILE EMBASE
               3   FILE ESBIOBASE
               1   FILE IFIPAT
               3   FILE IMSDRUGNEWS
              15   FILE INVESTEXT
               4   FILE LIFESCI
              13   FILE MEDLINE
               3   FILE NLDB
               4   FILE PASCAL
              11   FILE PCTFULL
               2   FILE PHIN
               1   FILE PROMT
              22   FILE SCISEARCH
               4   FILE TOXCENTER
               6   FILE USPATFULL
               2   FILE WPIDS
               2   FILE WPINDEX
L15             QUE BILN 2061
               ---------

     INDEX 'EMBASE, SCISEARCH, BIOSIS, INVESTEXT, MEDLINE, PCTFULL,
CAPLUS,
     DDFU, DRUGU, BIOTECHNO, USPATFULL, LIFESCI, PASCAL, TOXCENTER,
ESBIOBASE,
```

```
     IMSDRUGNEWS, NLDB, ADISCTI, BIOENG, CBNB, COMPENDEX, PHIN,
WPIDS,
     WPINDEX, BABS, CIN, EMBAL, IFIPAT, PROMT' ENTERED AT 15:26:20 ON
26 OCT
     2004
                 SEA L15 AND CRYSTAL?
               ---------
               4   FILE EMBASE
               3   FILE SCISEARCH
               9   FILE PCTFULL
               3   FILE BIOTECHNO
               6   FILE USPATFULL
L16             QUE L15 AND CRYSTAL?
               ---------

     FILE 'EMBASE, SCISEARCH, BIOTECHNO, PCTFULL, USPATFULL' ENTERED
AT
     15:27:48 ON 26 OCT 2004
L17            0 L16, DUP REM
L18           25 L16
L19           21 DUP REM L18 (4 DUPLICATES REMOVED)
L20            2 L19 AND PD<20030327

=> stnindex
ENTER FILE OR CLUSTER NAMES (NONE):all
FILE 'ENCOMPLIT' ACCESS NOT AUTHORIZED
FILE 'ENCOMPLIT2' ACCESS NOT AUTHORIZED
FILE 'ENCOMPPAT' ACCESS NOT AUTHORIZED
FILE 'ENCOMPPAT2' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS                          SINCE FILE
TOTAL
                                                 ENTRY
SESSION
FULL ESTIMATED COST                              16.52
112.45

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE
TOTAL
                                                 ENTRY
SESSION
CA SUBSCRIBER PRICE                               0.00      -
4.90

INDEX '1MOBILITY, 2MOBILITY, ABI-INFORM, ADISCTI, AEROSPACE,
AGRICOLA,
      ALUMINIUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE,
BABS,
      BIBLIODATA, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS,
BIOTECHABS,
      BIOTECHDS, BIOTECHNO, BLLDB, CABA, CANCERLIT, ...'
ENTERED AT 15:32:46 ON 26 OCT 2004

143 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.
```

```
=> ciluprevir/cn
FILE '1MOBILITY'
'CN' IS NOT A VALID FIELD CODE
                0 CILUPREVIR/CN
FILE '2MOBILITY'
'CN' IS NOT A VALID FIELD CODE
                0 CILUPREVIR/CN
FILE 'ABI-INFORM'
                0 CILUPREVIR/CN
FILE 'ADISCTI'
'CN' IS NOT A VALID FIELD CODE
                0 CILUPREVIR/CN
FILE 'AEROSPACE'
'CN' IS NOT A VALID FIELD CODE
                0 CILUPREVIR/CN
FILE 'AGRICOLA'
                0 CILUPREVIR/CN
FILE 'ALUMINIUM'
'CN' IS NOT A VALID FIELD CODE
                0 CILUPREVIR/CN
FILE 'ANABSTR'
                0 CILUPREVIR/CN
                0 CILUPREVIR/CN
FILE 'ANTE'
'CN' IS NOT A VALID FIELD CODE
                0 CILUPREVIR/CN
FILE 'APOLLIT'
'CN' IS NOT A VALID FIELD CODE
                0 CILUPREVIR/CN
FILE 'AQUALINE'
'CN' IS NOT A VALID FIELD CODE
                0 CILUPREVIR/CN
FILE 'AQUASCI'
'CN' IS NOT A VALID FIELD CODE
                0 CILUPREVIR/CN
FILE 'AQUIRE'
                0 CILUPREVIR/CN
FILE 'BABS'
'CN' IS NOT A VALID FIELD CODE
                0 CILUPREVIR/CN
FILE 'BIBLIODATA'
'CN' IS NOT A VALID FIELD CODE
                0 CILUPREVIR/CN
FILE 'BIOBUSINESS'
                0 CILUPREVIR/CN
FILE 'BIOCOMMERCE'
'CN' IS NOT A VALID FIELD CODE
                0 CILUPREVIR/CN
<------User Break------>

'CN' IS NOT A VALID FIELD CODE
                0 CILUPREVIR/CN
FILE 'BIOSIS'
                0 CILUPREVIR/CN
SEARCH ENDED BY USER
FILE 'BIOTECHABS'
SEARCH ENDED BY USER
```

```
=> ciluprevir/
FILE '1MOBILITY'
'CILUPREVIR/' IS NOT A VALID FIELD CODE
For a list of field codes for the current file, enter "HELP SFIELDS"
at an arrow prompt (=>).

=> ciluprevir
FILE '1MOBILITY'
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             0 CILUPREVIR
FILE '2MOBILITY'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'ABI-INFORM'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'ADISCTI'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'AEROSPACE'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'AGRICOLA'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'ALUMINIUM'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'ANABSTR'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'ANTE'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'APOLLIT'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'AQUALINE'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'AQUASCI'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'AQUIRE'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'BABS'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'BIBLIODATA'
             0 CILUPREVIR
FILE 'BIOBUSINESS'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'BIOCOMMERCE'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'BIOENG'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'BIOSIS'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'BIOTECHABS'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'BIOTECHDS'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'BIOTECHNO'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'BLLDB'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'CABA'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'CANCERLIT'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'CAOLD'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'CAPLUS'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'CASREACT'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'CBNB'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'CEABA-VTB'
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L21  QUE CILUPREVIR

=> d rank
F1            3   EMBASE
F2            2   ESBIOBASE
F3            2   MEDLINE
F4            2   SCISEARCH
F5            1   DDFU
F6            1   DRUGU


=> fil f1-6
COST IN U.S. DOLLARS                        SINCE FILE
TOTAL                                          ENTRY

SESSION                                          5.70
FULL ESTIMATED COST
118.15

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)  SINCE FILE
TOTAL                                          ENTRY

SESSION                                          0.00
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FILE 'SCISEARCH' ENTERED AT 15:39:01 ON 26 OCT 2004
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=> s l21
L22          10 L21

=> l22 and pd<20030327
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   2 FILES SEARCHED...
'20030327' NOT A VALID FIELD CODE
'20030327' NOT A VALID FIELD CODE
L23           1 L22 AND PD<20030327

=> d l23

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     on STN
AN   2004039472  EMBASE  Full-text
TI   Gateways to Clinical Trials.
AU   Bayes M.; Rabasseda X.; Prous J.R.
CS   M. Bayes, Prous Science, S.A., P.O. Box 540, 08080 Barcelona,
Spain.
     mbayes@prous.com
SO   Methods and Findings in Experimental and Clinical Pharmacology,
(
     2003) 25/10 (831-855).
     Refs: 145
     ISSN: 0379-0355  CODEN: MFEPDX
CY   Spain
DT   Journal; General Review
FS   030     Pharmacology
     037     Drug Literature Index
     038     Adverse Reactions Titles
LA   English
SL   English


=> FIL STNGUIDE
COST IN U.S. DOLLARS                                SINCE FILE
TOTAL
                                                      ENTRY
SESSION
FULL ESTIMATED COST                                    8.37
126.52

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE
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                                                      ENTRY
SESSION
CA SUBSCRIBER PRICE                                    0.00
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4.90

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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Oct 22, 2004 (20041022/UP).

=> l23 all
MISSING OPERATOR L23 ALL
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> d l23 all
YOU HAVE REQUESTED DATA FROM FILE 'EMBASE' - CONTINUE? (Y)/N:y


L23  ANSWER 1 OF 1  EMBASE  COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS
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     on STN
AN   2004039472  EMBASE  Full-text
TI   Gateways to Clinical Trials.
AU   Bayes M.; Rabasseda X.; Prous J.R.
CS   M. Bayes, Prous Science, S.A., P.O. Box 540, 08080 Barcelona,
Spain.
     mbayes@prous.com
SO   Methods and Findings in Experimental and Clinical Pharmacology,
(
     2003) 25/10 (831-855).
     Refs: 145
     ISSN: 0379-0355  CODEN: MFEPDX
CY   Spain
DT   Journal; General Review
FS   030     Pharmacology
     037     Drug Literature Index
     038     Adverse Reactions Titles
LA   English
SL   English
AB   Gateways to Clinical Trials is a guide to the most recent
     clinical trials in current literature and congresses. The data
     in the following tables has been retrieved from the Clinical
     Studies Knowledge Area of Prous Science Integrity®, the drug
     discovery and development portal, http://integrity.prous.com.
     This issue focuses on the following selection of drugs: Abetimus
     sodium, adalimumab, alefacept, alemtuzumab, almotriptan, AMGN-
     0007, anakinra, anti-CTLA-4 Mab, L-arginine hydrochloride,
     arzoxifene hydrochloride, astemizole, atazanavir sulfate,
     atlizumab; Belimumab, BG-9928, binodenoson, bosentan, botulinum
     toxin type B, bovine lactoferrin, BufferGel; Caspofungin
     acetate, ciclesonide, cilomilast, ciluprevir, clofarabine, CVT-
     3146; Darbepoetin alfa, desloratadine, diflomotecan, doripenem,
     dronedarone hydrochloride, drotrecogin alfa (activated), DT388-
     GM-CSF, duloxetine hydrochloride, E-5564, efalizumab,
     enfuvirtide, esomeprazole magnesium, estradiol acetate, ETC-642,
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     exenatide, exisulind, ezetimib; Febuxostat; Gallium maltolate,
     ganirelix acetate, garenoxacin mesilate, gefitinib; H11, HuMax;
     IL-15, IDD-1, IGIV-C, imatinib mesylate, ISIS-14803, ITF-1697,
     ivabradine hydrochloride; KRN-5500; L-365260, levetiracetam,
     levosimendan, licofelone, linezolid, LJP-1082, lopinavir
     lumiracoxib; MCC-478, melatonin, morphine hydrochloride,
     morphine-6-glucuronide, moxidectin; N-Acetylcarnosine,
     natalizumab, NM-702, NNC-05-1869, NSC-703940; Ocinaplon OM-89,
     omalizumab, omeprazole/sodium bicarbonate, OPC-28326,
     ospemifene; PEG-filgrastim peginterferon alfa-2a, pegsunercept,
     pirfenidone, pralmorelin, pregabalin; Recombinant glucagon-like
     peptide-1 (7-36) amide, repifermin, RSD-1235; S-8184,
     selodenoson, sodium dichloroacetate, suberanilohydroxamic acid;
     TAS-102, terfenadine, teriparatide, tipranavir troxacitabine;
     Ximelagatran; YM-337. .COPYRGT. 2003 Prous Science. All rights
     reserved.
CT   Medical Descriptors:
     *drug monitoring
     drug indication
     drug efficacy
     drug safety
     side effect: SI, side effect
     patient compliance
     drug tolerability
     liver toxicity: SI, side effect
     bleeding: SI, side effect
     disease exacerbation
     systemic lupus erythematosus: SI, side effect
     digestive system ulcer: SI, side effect
     neutropenia: SI, side effect
     teratogenicity: SI, side effect
     human
     clinical trial
     review
     Drug Descriptors:
     abetimus: CT, clinical trial
     abetimus: IV, intravenous drug administration
     adalimumab: AE, adverse drug reaction
     adalimumab: CT, clinical trial
     linezolid: CT, clinical trial
     alemtuzumab: CT, clinical trial
     ivabradine: CT, clinical trial
     ivabradine: IV, intravenous drug administration
     recombinant interleukin 1 receptor blocking agent: CT, clinical
trial
     recombinant interleukin 1 receptor blocking agent: IA,
intraarterial drug
     administration
     glucagon like peptide 1: CT, clinical trial
     glucagon like peptide 1: SC, subcutaneous drug administration
     astemizole: CT, clinical trial
     atazanavir: CT, clinical trial
     bosentan: CT, clinical trial
     botulinum toxin B: CT, clinical trial
     caspofungin: CT, clinical trial
     ciclesonide: CT, clinical trial
     cilomilast: CT, clinical trial
     efalizumab: CT, clinical trial
     imatinib: CT, clinical trial
     terfenadine: CT, clinical trial
     tipranavir: CT, clinical trial
     tipranavir: PO, oral drug administration
     ximelagatran: CT, clinical trial
     ximelagatran: PO, oral drug administration
     ym 337: CT, clinical trial
     moxidectin: CT, clinical trial
     estradiol: CT, clinical trial
     novel erythropoiesis stimulating protein: CT, clinical trial
     novel erythropoiesis stimulating protein: IV, intravenous drug
     administration
     novel erythropoiesis stimulating protein: SC, subcutaneous drug
     administration
     desloratadine: CT, clinical trial
     desloratadine: PO, oral drug administration
     diflomotecan: CT, clinical trial
     diflomotecan: IV, intravenous drug administration
     diflomotecan: PO, oral drug administration
     morphine: CT, clinical trial
     etiracetam: CT, clinical trial
     doripenem: CT, clinical trial
     duloxetine: CT, clinical trial
     unindexed drug
RN   (abetimus) 167362-48-3, 169147-32-4; (adalimumab) 331731-18-1;
(linezolid)
     165800-03-3; (alemtuzumab) 216503-57-0; (ivabradine) 148849-67-
6,
     148870-80-8, 155974-00-8; (glucagon like peptide 1) 89750-14-1;
     (astemizole) 68844-77-9; (atazanavir) 198904-31-3; (bosentan)
147536-97-8,
     157212-55-0; (caspofungin) 189768-38-5; (ciclesonide) 126544-47-
6;
     (cilomilast) 153259-65-5; (efalizumab) 214745-43-4; (imatinib)
     152459-95-5, 220127-57-1; (terfenadine) 50679-08-8; (tipranavir)
     174484-41-4; (ximelagatran) 192939-46-1, 260790-58-7;
(moxidectin)
     113507-06-5; (estradiol) 50-28-2; (desloratadine) 100643-71-8;
     (diflomotecan) 220997-97-7; (morphine) 52-26-6, 57-27-2;
(etiracetam)
     102767-28-2, 33996-58-6; (doripenem) 148016-81-3; (duloxetine)
     116539-59-4, 136434-34-9
CN   Ym 337


=> DIS HIST

     (FILE 'HOME' ENTERED AT 14:24:22 ON 26 OCT 2004)

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AQUALINE,
     AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS, BIOTECHABS,
BIOTECHDS,
     BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN,
CONFSCI, CROPB,
     CROPU, DDFB, DDFU, DGENE, DISSABS, ...' ENTERED AT 14:25:23 ON
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26 OCT 2004

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L1             1 S 300832-84-2/RN
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               DEL SEL Y
               SEL RN
               SET SMA LOGIN

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L2             QUE 300832-84-2/BI AND OPTICAL?/FA
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L3             0 S L1/BMF

     FILE 'CAPLUS' ENTERED AT 14:28:18 ON 26 OCT 2004
L4             0 S L1/BPN

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L5             0 S L1/IMF

     FILE 'CAPLUS' ENTERED AT 14:28:41 ON 26 OCT 2004
L6             1 S L1/PEP

     FILE 'CAPLUS' ENTERED AT 14:29:30 ON 26 OCT 2004
L7             0 S L1/PUR

     FILE 'CAPLUS' ENTERED AT 14:29:48 ON 26 OCT 2004
L8             6 S (L1/SPN OR L1/CPN)
L9             6 FOCUS L8 1-

     FILE 'REGISTRY' ENTERED AT 14:31:45 ON 26 OCT 2004

     FILE 'HCAPLUS' ENTERED AT 14:32:46 ON 26 OCT 2004
L10           15 S L1
L11            0 L10 AND CRYSTAL
L12            0 L10 AND CRYSTAL?
L13            0 L10 AND ALCOHOL
L14            3 L10 AND PD<20030327

     FILE 'HOME' ENTERED AT 14:39:45 ON 26 OCT 2004

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AGRICOLA,
     ALUMINIUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE,
BABS,
     BIBLIODATA, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS,
BIOTECHABS,
     BIOTECHDS, BIOTECHNO, BLLDB, CABA, CANCERLIT, ...' ENTERED AT
15:24:55 ON
     26 OCT 2004
               SEA BILN 2061
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              2   FILE ADISCTI
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AGRICOLA,
     ALUMINIUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE,
BABS,
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15:32:46 ON
     26 OCT 2004
               SEA CILUPREVIR/CN
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              0*  FILE 2MOBILITY
              0*  FILE ADISCTI
              0*  FILE AEROSPACE
              0*  FILE ALUMINIUM
              0*  FILE ANTE
              0*  FILE APOLLIT
              0*  FILE AQUALINE
              0*  FILE AQUASCI
              0*  FILE BABS
              0*  FILE BIBLIODATA
              0*  FILE BIOCOMMERCE
              0*  FILE BIOENG
               SEA CILUPREVIR/
              ---------
              0*  FILE 1MOBILITY
               SEA CILUPREVIR
              ---------
              1   FILE DDFU
              1   FILE DRUGU
              3   FILE EMBASE
              2   FILE ESBIOBASE
              2   FILE MEDLINE
              2   FILE SCISEARCH
L21            QUE CILUPREVIR
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     FILE 'EMBASE, ESBIOBASE, MEDLINE, SCISEARCH, DRUGU' ENTERED AT
15:39:01
     ON 26 OCT 2004
L22           10 S L21
L23            1 L22 AND PD<20030327

     FILE 'STNGUIDE' ENTERED AT 15:40:30 ON 26 OCT 2004

     FILE 'EMBASE' ENTERED AT 15:41:46 ON 26 OCT 2004

     FILE 'STNGUIDE' ENTERED AT 15:41:46 ON 26 OCT 2004

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---Logging off of STN---
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              1   FILE BABS
              2   FILE BIOENG
             18   FILE BIOSIS
              8   FILE BIOTECHNO
             10   FILE CAPLUS
              2   FILE CBNB
              1   FILE CIN
              2   FILE COMPENDEX
             10   FILE DDFU
             10   FILE DRUGU
              1   FILE EMBAL
             42   FILE EMBASE
              3   FILE ESBIOBASE
              1   FILE IFIPAT
              3   FILE IMSDRUGNEWS
             15   FILE INVESTEXT
              4   FILE LIFESCI
             13   FILE MEDLINE
              3   FILE NLDB
              4   FILE PASCAL
             11   FILE PCTFULL
              2   FILE PHIN
              1   FILE PROMT
             22   FILE SCISEARCH
              4   FILE TOXCENTER
              6   FILE USPATFULL
              2   FILE WPIDS
              2   FILE WPINDEX
L15            QUE BILN 2061
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     INDEX 'EMBASE, SCISEARCH, BIOSIS, INVESTEXT, MEDLINE, PCTFULL,
CAPLUS,
     DDFU, DRUGU, BIOTECHNO, USPATFULL, LIFESCI, PASCAL, TOXCENTER,
ESBIOBASE,
     IMSDRUGNEWS, NLDB, ADISCTI, BIOENG, CBNB, COMPENDEX, PHIN,
WPIDS,
     WPINDEX, BABS, CIN, EMBAL, IFIPAT, PROMT' ENTERED AT 15:26:20 ON
26 OCT
     2004
               SEA L15 AND CRYSTAL?
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              4   FILE EMBASE
              3   FILE SCISEARCH
              9   FILE PCTFULL
              3   FILE BIOTECHNO
              6   FILE USPATFULL
L16            QUE L15 AND CRYSTAL?
              ---------

     FILE 'EMBASE, SCISEARCH, BIOTECHNO, PCTFULL, USPATFULL' ENTERED
AT
     15:27:48 ON 26 OCT 2004
L17            0 L16, DUP REM
L18           25 L16
L19           21 DUP REM L18 (4 DUPLICATES REMOVED)
L20            2 L19 AND PD<20030327
```

```
=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS                            SINCE FILE
TOTAL
                                                  ENTRY
SESSION
FULL ESTIMATED COST                                0.12
130.58

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE
TOTAL
                                                  ENTRY
SESSION
CA SUBSCRIBER PRICE                                0.00      -
4.90

STN INTERNATIONAL LOGOFF AT 15:42:43 ON 26 OCT 2004
```

```
Connecting via Winsock to STN



Welcome to STN International!  Enter x:x

LOGINID:ssspta1653adk

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * *
* *

 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  Jul 12   BEILSTEIN enhanced with new display and select
options,
                   resulting in a closer connection to BABS
 NEWS  4  AUG 02   IFIPAT/IFIUDB/IFICDB reloaded with new search and
display
                   fields
 NEWS  5  AUG 02   CAplus and CA patent records enhanced with European
and Japan
                   Patent Office Classifications
 NEWS  6  AUG 02   The Analysis Edition of STN Express with Discover!
                   (Version 7.01 for Windows) now available
 NEWS  7  AUG 27   BIOCOMMERCE: Changes and enhancements to content
coverage
 NEWS  8  AUG 27   BIOTECHABS/BIOTECHDS: Two new display fields added
for legal
                   status data from INPADOC
 NEWS  9  SEP 01   INPADOC: New family current-awareness alert (SDI)
available
 NEWS 10  SEP 01   New pricing for the Save Answers for SciFinder
Wizard within
                   STN Express with Discover!
 NEWS 11  SEP 01   New display format, HITSTR, available in
WPIDS/WPINDEX/WPIX
 NEWS 12  SEP 27   STANDARDS will no longer be available on STN
 NEWS 13  SEP 27   SWETSCAN will no longer be available on STN

 NEWS EXPRESS   JULY 30 CURRENT WINDOWS VERSION IS V7.01, CURRENT
                MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
                AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
 NEWS HOURS     STN Operating Hours Plus Help Desk Availability
 NEWS INTER     General Internet Information
 NEWS LOGIN     Welcome Banner and News Items
 NEWS PHONE     Direct Dial and Telecommunication Network Access to
STN
 NEWS WWW       CAS World Wide Web Site (general information)

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  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * *
* *

FILE 'HOME' ENTERED AT 14:24:22 ON 26 OCT 2004

=> index biosci
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS                                    SINCE FILE
TOTAL                                                        ENTRY

SESSION
FULL ESTIMATED COST                                          0.42
0.42

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE,
AQUALINE,
      AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS, BIOTECHABS,
BIOTECHDS,
      BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN,
CONFSCI, CROPB,
      CROPU, DDFB, DDFU, DGENE, DISSABS, ...' ENTERED AT 14:25:23 ON
26 OCT 2004

75 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> fil reg
COST IN U.S. DOLLARS                                    SINCE FILE
TOTAL                                                        ENTRY

SESSION
FULL ESTIMATED COST                                          1.14
1.56

FILE 'REGISTRY' ENTERED AT 14:26:32 ON 26 OCT 2004
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STRUCTURE FILE UPDATES:   25 OCT 2004  HIGHEST RN 769101-30-6
DICTIONARY FILE UPDATES:  25 OCT 2004  HIGHEST RN 769101-30-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for
details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> S 300832-84-2/RN
L1            1 300832-84-2/RN

=> DEL SEL Y

=> SEL RN
E1 THROUGH E1 ASSIGNED

=> INDEX BEILSTEIN, GMELIN
COST IN U.S. DOLLARS                                    SINCE FILE
TOTAL                                                        ENTRY

SESSION
FULL ESTIMATED COST                                          0.92
2.48

INDEX 'BEILSTEIN, GMELIN' ENTERED AT 14:27:43 ON 26 OCT 2004

2 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> S E1 AND OPTICAL?/FA
FILE 'BEILSTEIN'
             0 300832-84-2/BI
               (300832-84-2/RN)
        753186 OPTICAL?/FA
             0 300832-84-2/BI AND OPTICAL?/FA
FILE 'GMELIN'
             0 300832-84-2/BI
               (300832-84-2/RN)
         12899 OPTICAL?/FA
             0 300832-84-2/BI AND OPTICAL?/FA

L2   QUE 300832-84-2/BI AND OPTICAL?/FA

=> DIS RANK
NO F-NUMBERS HAD GREATER THAN ZERO HITS


=> FIL CAPLUS
COST IN U.S. DOLLARS                                    SINCE FILE
TOTAL                                                        ENTRY

SESSION
FULL ESTIMATED COST                                          0.57
3.05

FILE 'CAPLUS' ENTERED AT 14:28:02 ON 26 OCT 2004
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FILE COVERS 1907 - 26 Oct 2004  VOL 141 ISS 18
FILE LAST UPDATED: 25 Oct 2004  (20041025/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> S L1/BMF
            15 L1
         52155 BMF/RL
L3           0 L1/BMF
               (L1 (L) BMF/RL)

=> FIL CAPLUS
COST IN U.S. DOLLARS                                    SINCE FILE
TOTAL                                                        ENTRY

SESSION
FULL ESTIMATED COST                                          2.26
5.31

FILE 'CAPLUS' ENTERED AT 14:28:18 ON 26 OCT 2004
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FILE COVERS 1907 - 26 Oct 2004 VOL 141 ISS 18
FILE LAST UPDATED: 25 Oct 2004 (20041025/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S L1/BPN
15 L1
102210 BPN/RL
L4 0 L1/BPN
(L1 (L) BPN/RL)

=> FIL CAPLUS
COST IN U.S. DOLLARS SINCE FILE
TOTAL
ENTRY
SESSION
FULL ESTIMATED COST 2.26
7.57

FILE 'CAPLUS' ENTERED AT 14:28:28 ON 26 OCT 2004
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FILE COVERS 1907 - 26 Oct 2004 VOL 141 ISS 18
FILE LAST UPDATED: 25 Oct 2004 (20041025/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S L1/IMF
15 L1
390491 IMF/RL
L5 0 L1/IMF
(L1 (L) IMF/RL)

=> FIL CAPLUS
COST IN U.S. DOLLARS SINCE FILE
TOTAL
ENTRY
SESSION
FULL ESTIMATED COST 2.26
9.83

FILE 'CAPLUS' ENTERED AT 14:28:41 ON 26 OCT 2004
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FILE COVERS 1907 - 26 Oct 2004 VOL 141 ISS 18
FILE LAST UPDATED: 25 Oct 2004 (20041025/ED)

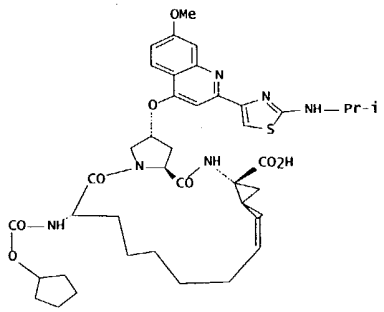
This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S L1/PEP
15 L1
1687596 PEP/RL
L6 1 L1/PEP
(L1 (L) PEP/RL)

=> DIS L6 1 CBIB ABS HITRN

L6 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
2004:310970 Document No. 140:327091 Potent inhibitor of HCV serine protease.
Chen, Shirlynn; Nehmiz, Gerhard; Croenlein, Jens Oliver; Steinmann,
Gerhard; Gunn, Jocelyn Abella; Costa, Phuong Do (Boehringer Ingelheim
International G.m.b.H., Germany). PCT Int. Appl. WO 2004030670 A1
20040415, 42 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA,
BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE,
EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP,
KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,

KZ, MD; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR,
GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR.
(English). CODEN: PIXXD2. APPLICATION: WO 2003-US30402 20030925.
PRIORITY: US 2002-PV414940 20020930; US 2002-PV421904 20021029; US
2002-PV433834 20021216; US 2003-PV443662 20030130.
GI



I

AB Disclosed are oral pharmaceutical compns., kits and methods of treating and preventing Hepatitis C Viral (HCV) infections wherein Compound (I), a potent inhibitor of HCV serine protease, or a pharmaceutically acceptable salt thereof, is administered in a selected dosage range. Also disclosed are the use of I or a pharmaceutically acceptable salt thereof, as a control substance for validating an HCV replication assay and also as a control substance for determining the relative effectiveness of one or more substances, alone or in combination, to inhibit the replication of HCV.
IT 300832-84-2
RL: PAC (Pharmacological activity); PEP (Physical, engineering or
chemical process); PYP (Physical process); THU (Therapeutic use);
BIOL (Biological study); PROC (Process); USES (Uses)
(potent inhibitor of HCV serine protease)

=> FIL CAPLUS
COST IN U.S. DOLLARS SINCE FILE
TOTAL
ENTRY
SESSION
FULL ESTIMATED COST 5.12
14.95

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE
TOTAL
ENTRY
SESSION
CA SUBSCRIBER PRICE -0.70
0.70

FILE 'CAPLUS' ENTERED AT 14:29:30 ON 26 OCT 2004
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FILE COVERS 1907 - 26 Oct 2004 VOL 141 ISS 18
FILE LAST UPDATED: 25 Oct 2004 (20041025/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S L1/PUR
15 L1
201134 PUR/RL
L7 0 L1/PUR
(L1 (L) PUR/RL)

=> FIL CAPLUS
COST IN U.S. DOLLARS SINCE FILE
TOTAL
ENTRY
SESSION
FULL ESTIMATED COST 2.26
17.21

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE
TOTAL
ENTRY
SESSION

CA SUBSCRIBER PRICE 0.00 -
0.70

FILE 'CAPLUS' ENTERED AT 14:29:48 ON 26 OCT 2004
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FILE COVERS 1907 - 26 Oct 2004 VOL 141 ISS 18
FILE LAST UPDATED: 25 Oct 2004 (20041025/ED)

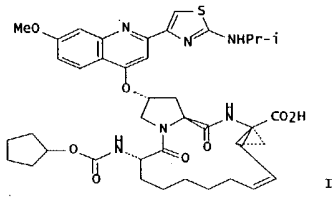
This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S (L1/SPN OR L1/CPN)
15 L1
1660968 SPN/RL
6 L1/SPN
(L1 (L) SPN/RL)
15 L1
1155 CPN/RL
0 L1/CPN
(L1 (L) CPN/RL)
L8 6 (L1/SPN OR L1/CPN)

=> FOCUS L8
PROCESSING COMPLETED FOR L8
L9 6 FOCUS L8 1-

=> DIS L9 1- CBIB ABS HITRN
YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):Y

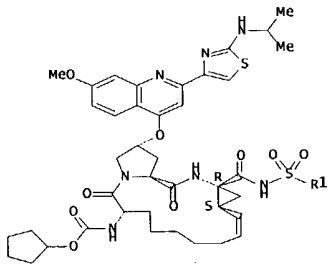
L9 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
2004:580783 Document No. 141:261053 Synthesis of BILN 2061, an HCV NS3
Protease Inhibitor with Proven Antiviral Effect in Humans.
Faucher,
Anne-Marie; Bailey, Murray D.; Beaulieu, Pierre L.; Brochu, Christian;
Duceppe, Jean-Simon; Ferland, Jean-Marie; Ghiro, Elise; Gorys, Vida;
Halmos, Ted; Kawai, Stephen H.; Poirier, Martin; Simoneau, Bruno;
Tsantrizos, Youla S.; Llinas-Brunet, Montse (Chemistry Department,
Boehringer Ingelheim (Canada) Ltd., Laval, QC, H7S 2G5, Can.). Organic
Letters, 6(17), 2901-2904 (English) 2004. CODEN: ORLEF7. ISSN: 1523-7060. Publisher: American Chemical Society.
GI



I

AB The synthesis of BILN 2061 (I), a hepatitis C virus (HCV) NS3 protease inhibitor with proven antiviral effect in humans, was accomplished in a convergent manner from four building blocks. The procedure described here was suitable for the preparation of multigram quantities of BILN 2061 for preclin. pharmacol. evaluation.
IT 300832-84-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(preparation of peptidyl macrocycle BILN-2061, an HCV NS3 protease inhibitor
with proven antiviral effect in humans)

L9 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
2004:370958 Document No. 140:357673 Preparation of macrocyclic peptides
active against the hepatitis C virus. Llinas-Brunet, Montse; Bailey,
Murray D. (Boehringer Ingelheim International G.m.b.h., Germany). PCT
Int. Appl. WO 2004037855 A1 20040506, 40 pp. DESIGNATED STATES: W: AE,
AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID,
IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD,
SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD; RW: AT, BE, BF, BJ, CF, CG, CH, CI,
CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL,
PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2.
APPLICATION: WO
2003-CA1604 20031020. PRIORITY: US 2002-PV421414 20021025; US 2002-PV433820 20021216; US 2003-PV442768 20030127.
GI

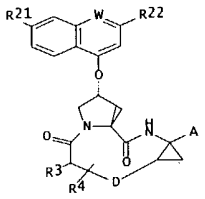


I

AB Macrocyclic peptides I [R1 is (un)substituted alkyl, cycloalkyl, alkylcycloalkyl, aryl or heteroaryl] or their pharmaceutically-acceptable salts were prepared as inhibitors of the hepatitis C virus (HCV) NS3 protease. Thus, I (R = Me) was prepared by a multistep sequence involving peptide coupling, olefin metathesis to form the macrocycle and methanesulfonamidation.
IT 300832-84-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of macrocyclic peptides active against the hepatitis C virus)

L9 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
2004:168624 Document No. 140:350045 Structure-activity study on a novel
series of macrocyclic inhibitors of the hepatitis C virus NS3 protease
leading to the discovery of BILN 2061. Llinas-Brunet, Montse; Bailey,
Murray D.; Bolger, Gordon; Brochu, Christian; Faucher, Anne-Marie;
Ferland, Jean Marie; Garneau, Michel; Ghiro, Elise; Gorys, Vida;
Grand-Maitre, Chantal; Halmos, Ted; Lapeyre-Paquette, Nicole; Liard,
Francine; Poirier, Martin; Rheaume, Manon; Tsantrizos, Youla S.; Lamarre,
Daniel (Departments of Chemistry and Biological Sciences, Boehringer
Ingelheim (Canada) Ltd., Laval, QC, H7S 2G5, Can.). Journal of Medicinal
Chemistry, 47(7), 1605-1608 (English) 2004. CODEN: JMCMAR. ISSN:
0022-2623. Publisher: American Chemical Society.
AB From the discovery of competitive hexapeptide inhibitors, potent and selective HCV NS3 protease macrocyclic inhibitors have been identified. Structure-activity relationship studies were performed focusing on optimizing the N-terminal carbamate and the aromatic substituent on the (4R)-hydroxyproline moiety. Inhibitors meeting the potency criteria in the cell-based assay and with improved oral bioavailability in rats were identified. BILN 2061 was selected as the best compound, the first NS3 protease inhibitor reported with antiviral activity in man.
IT 300832-84-2P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic
preparation); BIOL (Biological study); PREP (Preparation)
(BILN 2061; structure-activity study on a novel series of macrocyclic
inhibitors of the hepatitis C virus NS3 protease leading to the
discovery of BILN 2061)

L9 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
2003:648255 Document No. 139:197768 Preparation of macrocyclic peptides
active against the hepatitis C virus. Tsantrizos, Youla S.; Cameron, Dale
R.; Faucher, Anne-Marie; Ghiro, Elise; Goudreau, Nathalie; Halmos, Teddy;
Llinas-Brunet, Montse (Boehringer Ingelheim (Canada) Ltd., Can.). U.S. US
6608027 B1 20030819, 90 pp., Cont.-in-part of U.S. Ser. No. 542,675,
abandoned. (English). CODEN: USXXAM. APPLICATION: US 2001-760946
20010116. PRIORITY: US 1999-PV128011 19990406; US 2000-542675 20000403.
GI



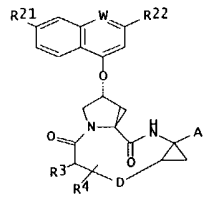
I

AB Macrocyclic peptides I [W = CH or N; R21 = H, halo, alkyl, cycloalkyl, haloalkyl, alkoxy, cycloalkoxy, hydroxy, or an amino group; R22 = H, halo, alkyl, cycloalkyl, haloalkyl, thioalkyl, alkoxy, cycloalkoxy, alkoxyalkyl, cycloalkyl, aryl or heteroaryl; R3 = hydroxy, NH2, aryl- or heteroarylamino, NHCOR32, CONHR32, CO2R32, where R32 is alkyl or cycloalkyl; D is a 5 to 10-atom saturated or unsatd. alkylene chain optionally containing one to three heteroatoms independently selected from: O, S, or NH or substituted imino; R4 = H or from one to three substituents at any carbon atom of chain D; A is an amide or carboxylic acid group or a pharmaceutically acceptable salt or ester; two diastereomers may exist at the cyclopropane moiety] were prepared which are active in-vitro and in cellular assays against the NS3 protease of the hepatitis C virus. Thus, macrocyclic peptide I [W = N; R21, R22, R4 = H; A = CO2H; R3CH-D = (S)-(Me3CO2CNH)CH(CH2)3CH:CH(CH2)2-E (syn to acid)] was prepared and showed IC50 > 0.1 μM in the full-length NS3-NS4A heterodimer protein fluorogenic assay.

IT 300832-84-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(preparation of macrocyclic peptides active against the hepatitis C virus)

L9 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
2003:511084 Document No. 139:69527 Preparation of macrocyclic compounds as
inhibitors of hepatitis C virus. Campbell, Jeffrey Allen; Good, Andrew
Charles (Bristol-Myers Squibb Company, USA). PCT Int. Appl. WO 2003053349
A2 20030703, 225 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ,
BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC,
EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP,
KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO,
NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW:
AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR,
IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN:
PIXXD2. APPLICATION: WO 2000-CA353 20000403. PRIORITY: US 1999-PV128011
19990406.

GI



I

AB Macrocyclic peptides I [W = CH or N; R21 = H, halo, alkyl, cycloalkyl, haloalkyl, alkoxy, cycloalkoxy, hydroxy, or an amino group; R22 = H, halo, alkyl, cycloalkyl, haloalkyl, thioalkyl, alkoxy, cycloalkoxy, alkoxyalkyl, cycloalkyl, aryl or heteroaryl; R3 = hydroxy, NH2, aryl- or heteroarylamino, NHCOR32, CONHR32, CO2R32, where R32 is alkyl or cycloalkyl; D is a 5 to 10-atom saturated or unsatd. alkylene chain optionally containing one to three heteroatoms independently selected from: O, S, or NH or substituted imino; R4 = H or from one to three substituents at any carbon atom of chain D; A is an amide or carboxylic acid group or a pharmaceutically acceptable salt or ester; two diastereomers may exist at the cyclopropane moiety] were prepared which are active in-vitro and in cellular assays against the NS3 protease of the hepatitis C virus . Thus, macrocyclic peptide I [W = N; R21, R22, R4 = H; A = CO2H; R3CH-D = (S)-(Me3CO2CNH)CH(CH2)3CH:CH(CH2)2-E (syn to acid)] was prepared and showed IC50 > 0.1 μM in the full-length NS3-NS4A heterodimer protein fluorogenic assay.

IT 300832-84-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(preparation of macrocyclic peptides active against the hepatitis C virus)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to macrocyclic compds. I [R1 = (cyclo)alkyl; R2 = H, halo, alkyl, alkoxy, cycloalkoxy, (un)substituted aryl or heterocyclyl; R3 = H, halo, CF3, alkoxy, cycloalkoxy; R4 = NH2 or NHR6, where R6 is alkanoyl, alkylaminocarbonyl, or carbalkoxy; Q is a 3-9 atom (un)saturated alkylene chain optionally containing 1-3 heteroatoms O, S, SO, or SO2], including methods for their synthesis and use in pharmaceutical compns. for therapeutic or prophylactic prevention or treatment of hepatitis C virus (HCV) infection. Thus, 3,13-diazatricyclo[11.3.0.04,6]hexadec-7-ene derivative II was prepared by a multistep procedure and assayed for inhibition of HCV NS3/4A protease (IC50 < 5 μM).

IT 300832-84-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of macrocyclic compds. as inhibitors of hepatitis C virus)

L9 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
2000:725652 Document No. 133:296659 Preparation of macrocyclic peptides
active against the hepatitis C virus. Tsantrizos, Youla S.; Cameron, Dale
R.; Faucher, Anne-marie; Ghiro, Elise; Goudreau, Nathalie; Halmos, Teddy;
Llinas-brunet, Montse (Boehringer Ingelheim (Canada) Ltd., Can.). PCT
Int. Appl. WO 2000059929 A1 20001012, 154 pp. DESIGNATED STATES: W: AE,
AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE,
DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
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(Uses)
(preparation of macrocyclic peptides active against the hepatitis C virus)

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FILE 'REGISTRY' ENTERED AT 14:31:45 ON 26 OCT 2004
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STRUCTURE FILE UPDATES: 25 OCT 2004 HIGHEST RN 769101-30-6
DICTIONARY FILE UPDATES: 25 OCT 2004 HIGHEST RN 769101-30-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

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Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d his

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CROPU, DDFB, DDFU, DGENE, DISSABS, ...' ENTERED AT 14:25:23 ON 26 OCT 2004

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FILE COVERS 1907 - 26 Oct 2004  VOL 141 ISS 18
FILE LAST UPDATED: 25 Oct 2004  (20041025/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


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        600101 CRYSTALS
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L11          0 L10 AND CRYSTAL

=> l10 and crystal?
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L12          0 L10 AND CRYSTAL?

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L14  ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:        2004:252197  HCAPLUS Full-text
DOCUMENT NUMBER:         140:281350
TITLE:                   Spiro compounds for inhibiting the first-
pass effect
INVENTOR(S):             Harris, James W.
PATENT ASSIGNEE(S):      Bioavailability System, LLC, USA
SOURCE:                  U.S. Pat. Appl. Publ., 133 pp., Cont.-in-
part of U.S.
                         Ser. No. 793,416.
                         CODEN: USXXCO
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  5
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L14  ANSWER 2 OF 3  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:        2003:886572  HCAPLUS Full-text
DOCUMENT NUMBER:         140:122161
TITLE:                   An NS3 protease inhibitor with antiviral
effects in
                         humans infected with hepatitis C virus
AUTHOR(S):               Lamarre, Daniel; Anderson, Paul C.; Bailey,
Murray;
                         Beaulieu, Pierre; Bolger, Gordon; Bonneau,
Pierre;
                         Boes, Michael; Cameron, Dale R.; Cartier,
Mireille;
                         Cordingley, Michael G.; Faucher, Anne-Marie;
Goudreau,
                         Nathalie; Kawai, Stephen H.; Kukolj, George;
Lagace,
                         Lisette; LaPlante, Steven R.; Narjes, Hans;
Poupart,
                         Marc-Andre; Rancourt, Jean; Sentjens, Roel
E.; St.
                         George, Roger; Simoneau, Bruno; Steinmann,
Gerhard;
                         Thibeault, Diane; Tsantrizos, Youla S.;
Weldon, Steven
                         M.; Yong, Chan-Loi; Llinas-Brunet, Montse
CORPORATE SOURCE:        Departments of Biological Sciences,
Boehringer
                         Ingelheim (Canada) Ltd, Laval, QC, H7S 2G5,
Can.
SOURCE:                  Nature (London, United Kingdom) (2003),
                         426(6963), 186-189
                         CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER:               Nature Publishing Group
DOCUMENT TYPE:           Journal
LANGUAGE:                English
REFERENCE COUNT:         30     THERE ARE 30 CITED REFERENCES
AVAILABLE FOR THIS
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L14  ANSWER 3 OF 3  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:        2000:725652  HCAPLUS Full-text
DOCUMENT NUMBER:         133:296659
TITLE:                   Preparation of macrocyclic peptides active
against the
                         hepatitis C virus
INVENTOR(S):             Tsantrizos, Youla S.; Cameron, Dale R.;
Faucher,
                         Anne-marie; Ghiro, Elise; Goudreau,
Nathalie; Halmos,
                         Teddy; Llinas-brunet, Montse
PATENT ASSIGNEE(S):      Boehringer Ingelheim (Canada) Ltd., Can.
SOURCE:                  PCT Int. Appl., 154 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
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FAMILY ACC. NUM. COUNT:  2
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SD, SE,
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20011004 <--
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20011005 <--
PRIORITY APPLN. INFO.:                         US 1999-128011P      P
19990406
                                               EP 2000-913999       A3
20000403
                                               WO 2000-CA353        W
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OTHER SOURCE(S):           MARPAT 133:296659
REFERENCE COUNT:           1       THERE ARE 1 CITED REFERENCES AVAILABLE
FOR THIS
                                   RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT


=> d l14 1 hitstr

L14  ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2004 ACS on STN
IT   300832-84-2, BILN 2061
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
       (spiro compds. for inhibiting the first-pass effect)
RN   300832-84-2  HCAPLUS
CN   Cyclopropa[e]pyrrolo[1,2-a][1,4]diazacyclopentadecine-14a(5H)-
carboxylic
     acid, 6-[[(cyclopentyloxy)carbonyl]amino]-
1,2,3,6,7,8,9,10,11,13a,14,15,16
     ,16a-tetradecahydro-2-[[7-methoxy-2-[2-[(1-methylethyl)amino]-4-
thiazolyl]-
     4-quinolinyl]oxy]-5,16-dioxo-, (2R,6S,12Z,13aS,14aR,16aS)- (9CI)
(CA
     INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.
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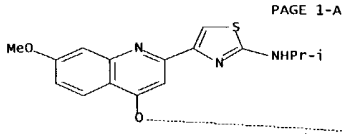
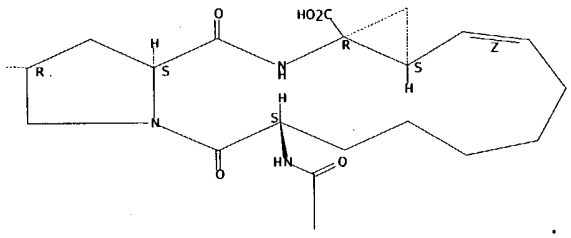
PAGE 1-A



PAGE 1-B



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BABS,
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BIOTECHABS,
       BIOTECHDS, BIOTECHNO, BLLDB, CABA, CANCERLIT, ...'
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143 FILES IN THE FILE LIST IN STNINDEX

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L15  QUE BILN 2061

=> d rank
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F2          22   SCISEARCH
F3          18   BIOSIS
F4          15   INVESTEXT
F5          13   MEDLINE
F6          11   PCTFULL
F7          10   CAPLUS
F8          10   DDFU
F9          10   DRUGU
F10          8   BIOTECHNO
F11          6   USPATFULL
F12          4   LIFESCI
F13          4   PASCAL
F14          4   TOXCENTER
F15          3   ESBIOBASE
F16          3   IMSDRUGNEWS
F17          3   NLDB
F18          2   ADISCTI
F19          2   BIOENG
F20          2   CBNB
F21          2   COMPENDEX
F22          2   PHIN
F23          2   WPIDS
F24          2   WPINDEX
F25          1   BABS
F26          1   CIN
F27          1   EMBAL
F28          1   IFIPAT
F29          1   PROMT
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=> index f1-f29
COST IN U.S. DOLLARS                          SINCE FILE
TOTAL                                            ENTRY

SESSION
FULL ESTIMATED COST                               1.14
94.22

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE
TOTAL                                            ENTRY

SESSION
CA SUBSCRIBER PRICE                               0.00
4.90

INDEX 'EMBASE, SCISEARCH, BIOSIS, INVESTEXT, MEDLINE, PCTFULL,
CAPLUS, DDFU,
      DRUGU, BIOTECHNO, USPATFULL, LIFESCI, PASCAL, TOXCENTER,
ESBIOBASE,
      IMSDRUGNEWS, NLDB, ADISCTI, BIOENG, CBNB, COMPENDEX, PHIN,
WPIDS,
      WPINDEX, BABS, CIN, EMBAL, IFIPAT, PROMT' ENTERED AT 15:26:20
ON 26 OCT 2004

29 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> d his l14-

     (FILE 'HCAPLUS' ENTERED AT 14:32:46 ON 26 OCT 2004)
L14             3 L10 AND PD<20030327

     FILE 'HOME' ENTERED AT 14:39:45 ON 26 OCT 2004

     INDEX '1MOBILITY, 2MOBILITY, ABI-INFORM, ADISCTI, AEROSPACE,
AGRICOLA,
     ALUMINIUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE,
BABS,
     BIBLIODATA, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS,
BIOTECHABS,
     BIOTECHDS, BIOTECHNO, BLLDB, CABA, CANCERLIT, ...' ENTERED AT
15:24:55 ON
     26 OCT 2004
               SEA BILN 2061
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               2   FILE ADISCTI
               1   FILE BABS
               2   FILE BIOENG
              18   FILE BIOSIS
               8   FILE BIOTECHNO
              10   FILE CAPLUS
               2   FILE CBNB
               1   FILE CIN
               2   FILE COMPENDEX
              10   FILE DDFU
              10   FILE DRUGU
               1   FILE EMBAL
              42   FILE EMBASE
               3   FILE ESBIOBASE
               1   FILE IFIPAT
               3   FILE IMSDRUGNEWS
              15   FILE INVESTEXT
               4   FILE LIFESCI
              13   FILE MEDLINE
               3   FILE NLDB
               4   FILE PASCAL
              11   FILE PCTFULL
               2   FILE PHIN
               1   FILE PROMT
              22   FILE SCISEARCH
               4   FILE TOXCENTER
               6   FILE USPATFULL
               2   FILE WPIDS
               2   FILE WPINDEX
L15             QUE BILN 2061
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     INDEX 'EMBASE, SCISEARCH, BIOSIS, INVESTEXT, MEDLINE, PCTFULL,
CAPLUS,
     DDFU, DRUGU, BIOTECHNO, USPATFULL, LIFESCI, PASCAL, TOXCENTER,
ESBIOBASE,
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WPIDS,
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26 OCT
     2004

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F2            6   USPATFULL
F3            4   EMBASE
F4            3   SCISEARCH
F5            3   BIOTECHNO


=> file f3-5,f1,f2
COST IN U.S. DOLLARS                                SINCE FILE
TOTAL                                                  ENTRY

SESSION
FULL ESTIMATED COST                                      1.71
95.93

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE
TOTAL                                                  ENTRY

SESSION
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=> l16, dup rem
L17           0 L16, DUP REM
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=> l16
L18          25 L16

=> dup rem
ENTER L# LIST OR (END):l18
PROCESSING COMPLETED FOR L18
L19          21 DUP REM L18 (4 DUPLICATES REMOVED)

=> l19 and pd<20030327
   1 FILES SEARCHED...
   3 FILES SEARCHED...
L20           2 L19 AND PD<20030327

=> d l20 1-2 ibib hitstr abs kwic
'HITSTR' IS NOT A VALID FORMAT FOR FILE 'EMBASE'

The following are valid formats:

The default display format is BIB.

ABS --------- AB
ALL --------- AN, DN, TI, AU, CS, SO, PUI, CY, DT, FS, LA, SL, AB,
              CT, RN, CN, NP, CO, GEN
BIB --------- AN, DN, TI, AU, CS, SO, PUI, CY, DT, FS, LA, SL
CBIB -------- Compressed bibliographic data
DALL -------- ALL, delimited for post-processing
IABS -------- ABS, with a text label
IALL -------- ALL, indented with text labels
IBIB -------- BIB, indented with text labels
IND --------- CT, RN, CN, NP, CO, GEN
TRIAL ------  TI, CT, RN, CN, NP, CO, GEN
 (SAM, TRI)
HIT --------- All fields containing hit terms
HITIND ------ IND
KWIC -------- All hit terms plus 20 words on either side
OCC --------- List of display fields containing hit terms
              and number of occurrences in each field

Hit terms will be highlighted in all displayable fields.

To display a particular field or fields,  enter the display field
codes.  For a list of display field codes, enter 'HELP DFIELDS'
at an arrow prompt (=>).  Examples of formats include: 'BIB';
'AB'; 'SO,ST'.  You may specify the format fields in any order,
and the information will be displayed in the same order as the
format specification.

The same formats (except for HIT, HITIND, KWIC, and OCC) may be
used with the DISPLAY ACC command to display the record for a
specified Accession Number.

ENTER DISPLAY FORMAT (BIB):iall

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     on STN

ACCESSION NUMBER:    2003468113  EMBASE  Full-text
TITLE:               Current therapy and new molecular approaches to
antiviral
                     treatment and prevention of hepatitis C.
AUTHOR:              Hugle T.; Cerny A.
CORPORATE SOURCE:    Dr. A. Cerny, Clinica Medica, Ospedale Civico,
CH-6903
                     Lugano, Switzerland. andreas.cerny@bluewin.ch
SOURCE:              Reviews in Medical Virology, (2003) 13/6
                     (361-371).
                     Refs: 79
                     ISSN: 1052-9276  CODEN: RMVIEW
COUNTRY:             United Kingdom
DOCUMENT TYPE:       Journal; General Review
FILE SEGMENT:        004     Microbiology
                     030     Pharmacology
                     037     Drug Literature Index
                     038     Adverse Reactions Titles
                     039     Pharmacy
LANGUAGE:            English
SUMMARY LANGUAGE:    English
ABSTRACT:
Current therapeutic options for hepatitis C are limited, especially
for
genotype 1. For genotypes 2 and 3, pegylated interferon in
combination with
ribavirin, can lead to a sustained virological response in up to 80%
of
patients. Unfortunately, adverse effects of IFN and ribavirin are a
major
problem and the list of contraindications for HCV therapy is long,
including
decompensated cirrhosis of the liver and psychiatric disorders.
Therefore,
alternative therapeutic approaches are needed. New delivery options
for IFN and
ribavirin are aimed at optimising efficiency and reducing adverse
effects.
Recent progress in the molecular virology of HCV has identified new
targets for
antiviral intervention. Inhibition of HCV gene expression and
replication as
well as immunotherapeutic concepts aimed at enhancing the cellular
immune
response against HCV are being explored. Solution of the crystal
structures of HCV key enzymes led to the design of specific
inhibitors
including compounds active against the well characterised NS3 serine
protease
and RNA-dependent RNA polymerase which are currently in the early
phase
clinical investigation. New strategies for inhibiting HCV gene
expression
include the use of antisense oligodeoxynucleotides and ribozymes.
Immunomodulation by agents such as inosine monophosphate
dehydrogenase
inhibitors, thymosin-alpha 1, histamine or amantadine are being
```

studied in
combination with IFN and/or ribavirin. Immunotherapeutic vaccination
with
recombinant HCV E1 protein improved host immunity against HCV and
thus seems to
be a promising new option. Copyright .COPYRGT. 2003 John Wiley &
Sons, Ltd.

CONTROLLED TERM: Medical Descriptors:
*hepatitis C: DT, drug therapy
*hepatitis C: ET, etiology
*hepatitis C: PC, prevention
*infection prevention
virus gene
genotype
drug response
drug contraindication
drug delivery system
side effect: SI, side effect
gene expression
drug targeting
immunotherapy
enzyme structure
crystal structure
drug design
drug activity
antiviral activity
protein targeting
immunomodulation
vaccination
Hepatitis C virus
immune response
cellular immunity
hemolytic anemia: SI, side effect
mental disease: SI, side effect
flu like syndrome: SI, side effect
leukopenia: SI, side effect
thrombocytopenia: SI, side effect
teratogenicity
virus replication
drug hypersensitivity: SI, side effect
rash: SI, side effect
human
nonhuman
clinical trial
review
Drug Descriptors:
alpha interferon: AE, adverse drug reaction
alpha interferon: CT, clinical trial
alpha interferon: CB, drug combination
alpha interferon: DT, drug therapy
alpha interferon: TO, drug toxicity
alpha interferon: PR, pharmaceutics
alpha interferon: PD, pharmacology
alpha interferon: SC, subcutaneous drug
administration
ribavirin: AE, adverse drug reaction
ribavirin: CT, clinical trial
ribavirin: CB, drug combination
ribavirin: CM, drug comparison
ribavirin: DT, drug therapy
ribavirin: PK, pharmacokinetics
ribavirin: PD, pharmacology
ribavirin: PO, oral drug administration
albumin conjugate: PR, pharmaceutics
liposome: PR, pharmaceutics
polyaminoacid: PR, pharmaceutics
polyaminoacid: PO, oral drug administration
ribavirin derivative: AE, adverse drug reaction
ribavirin derivative: CT, clinical trial
ribavirin derivative: CB, drug combination
ribavirin derivative: CM, drug comparison
ribavirin derivative: DT, drug therapy
ribavirin derivative: PD, pharmacology
viramidine: AE, adverse drug reaction
viramidine: CT, clinical trial
viramidine: CB, drug combination
viramidine: CM, drug comparison
viramidine: DT, drug therapy
viramidine: PD, pharmacology
levovirin: AE, adverse drug reaction
levovirin: CT, clinical trial
levovirin: CM, drug comparison
levovirin: DT, drug therapy
levovirin: PD, pharmacology
proteinase inhibitor: AE, adverse drug reaction
proteinase inhibitor: CT, clinical trial
proteinase inhibitor: DO, drug dose
proteinase inhibitor: DT, drug therapy
proteinase inhibitor: PK, pharmacokinetics
proteinase inhibitor: PD, pharmacology
proteinase inhibitor: PO, oral drug
administration
biln 2061: AE, adverse drug reaction
biln 2061: CT, clinical trial
biln 2061: DO, drug dose
biln 2061: DT, drug therapy
biln 2061: PK, pharmacokinetics
biln 2061: PD, pharmacology
biln 2061: PO, oral drug administration
vx 950: DT, drug therapy
vx 950: PD, pharmacology
virus protein
protein NS5B
RNA directed DNA polymerase inhibitor: CT,
clinical trial
RNA directed DNA polymerase inhibitor: DT, drug
therapy
RNA directed DNA polymerase inhibitor: PD,
pharmacology
jtk 003: CT, clinical trial
jtk 003: DT, drug therapy
jtk 003: PD, pharmacology
ribozyme: AE, adverse drug reaction
ribozyme: CT, clinical trial
ribozyme: DT, drug therapy
ribozyme: TO, drug toxicity
ribozyme: PD, pharmacology
hepatozyme: AE, adverse drug reaction
hepatozyme: CT, clinical trial
hepatozyme: DT, drug therapy
hepatozyme: TO, drug toxicity
hepatozyme: PD, pharmacology
antisense oligodeoxynucleotide: CT, clinical
trial
antisense oligodeoxynucleotide: DT, drug therapy
antisense oligodeoxynucleotide: PD, pharmacology
isis 14803: CT, clinical trial
isis 14803: DT, drug therapy
isis 14803: PD, pharmacology
RNA derivative: DV, drug development
RNA derivative: DT, drug therapy
RNA derivative: PD, pharmacology
small interfering rna: DV, drug development
small interfering rna: DT, drug therapy
small interfering rna: PD, pharmacology
monoclonal antibody: DT, drug therapy
monoclonal antibody: PD, pharmacology
xtl 002: DT, drug therapy
xtl 002: PD, pharmacology
cicavir: DT, drug therapy
cicavir: PD, pharmacology
immunomodulating agent: CB, drug combination
immunomodulating agent: DT, drug therapy
thymosin alpha1: CT, clinical trial
thymosin alpha1: CB, drug combination
thymosin alpha1: DO, drug dose
thymosin alpha1: DT, drug therapy
thymosin alpha1: PD, pharmacology
inosinate dehydrogenase inhibitor: CB, drug
combination
inosinate dehydrogenase inhibitor: DT, drug
therapy
inosinate dehydrogenase inhibitor: PD,
pharmacology
merimepodib: CT, clinical trial
merimepodib: CB, drug combination
merimepodib: DT, drug therapy
merimepodib: PD, pharmacology
unindexed drug
unclassified drug
CAS REGISTRY NO.: (ribavirin) 36791-04-5; (proteinase inhibitor)
37205-61-1;
(thymosin alpha1) 69521-94-4; (merimepodib)
198821-22-6,
198821-38-4
CHEMICAL NAME: (1) Vx 950; (2) Jtk 003; Biln 2061; Isis 14803;
Xtl 002
COMPANY NAME: (1) Vertex; (2) Akros; Ribozyme Pharmaceuticals;
NABI;
Sciclone; RegeneRx; Maxim

L20 ANSWER 2 OF 2 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS
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ACCESSION NUMBER: 2003195244 EMBASE Full-text
TITLE: Hepatitis C virus therapies: Current treatments,
targets
and future perspectives.
AUTHOR: Walker M.P.; Appleby T.C.; Zhong W.; Lau J.Y.N.;
Hong Z.
CORPORATE SOURCE: Z. Hong, Ribapharm Inc., Hyland Avenue, Costa
Mesa, CA,
United States. zhihong@ribapharm.com
SOURCE: Antiviral Chemistry and Chemotherapy, (2003) 14/1
(1-21).
Refs: 208
ISSN: 0956-3202 CODEN: ACCHEH
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Chronic hepatitis C virus (HCV) infection is the cause of an emerging
global
epidemic of chronic liver disease. Current combination therapies are
at best
80% efficacious and are often poorly tolerated. Strategies to improve
the
therapeutic response include the development of novel interferons,
nucleoside
analogues with reduced haemolysis compared with ribavirin and inosine
5'-monophosphate dehydrogenase inhibitors. Compounds in preclinical
or early
clinical trials include small molecules that inhibit virus-specific
enzymes
(such as the serine proteases, RNA polymerase and helicase) or
interfere with
translation (including antisense molecules, iRNA and ribozymes).
Advances in
understanding HCV replication, obtaining a sub-genomic replicon and
contriving
potential small animal models, in addition to solving
crystallographic
structures for the replication enzymes, have improved prospects for
developing
novel therapies. This review summarizes current and evolving
treatments for
chronic hepatitis C infection. In addition, progress in HCV targets
and drug
discovery tools valuable in the search for novel anti-HCV agents is
detailed.

CONTROLLED TERM: Medical Descriptors:
*hepatitis C: DT, drug therapy
*hepatitis C: EP, epidemiology
*hepatitis C: ET, etiology
*chronic liver disease: ET, etiology
drug efficacy
drug tolerance
hemolytic anemia: SI, side effect
side effect: SI, side effect
alanine aminotransferase blood level
virus replication
replicon
crystal structure
RNA translation
untranslated region
internal ribosome entry site
monotherapy
virus load
treatment outcome
treatment indication
immunomodulation
drug safety
treatment failure
chimpanzee
transgenic mouse
Hepatitis GB virus B
IC 50
structure activity relation
drug structure
virus assembly
human
nonhuman
clinical trial
review
priority journal
Drug Descriptors:
*antivirus agent: AE, adverse drug reaction
*antivirus agent: CT, clinical trial
*antivirus agent: AN, drug analysis
*antivirus agent: CB, drug combination
*antivirus agent: CM, drug comparison
*antivirus agent: DV, drug development
*antivirus agent: DO, drug dose
*antivirus agent: DT, drug therapy
*antivirus agent: PD, pharmacology
*antivirus agent: IV, intravenous drug

administration

*antivirus agent: SC, subcutaneous drug

administration

alpha interferon: AE, adverse drug reaction
alpha interferon: CB, drug combination
alpha interferon: CM, drug comparison
alpha interferon: DO, drug dose
alpha interferon: DT, drug therapy
alpha interferon: PD, pharmacology
nucleoside derivative: AN, drug analysis
nucleoside derivative: CM, drug comparison

nucleoside derivative: DV, drug development
nucleoside derivative: PR, pharmaceutics
nucleoside derivative: PD, pharmacology
ribavirin: AE, adverse drug reaction
ribavirin: CT, clinical trial
ribavirin: CB, drug combination
ribavirin: CM, drug comparison
ribavirin: DO, drug dose
ribavirin: DT, drug therapy
ribavirin: PD, pharmacology
inosinate dehydrogenase inhibitor: CM, drug

comparison

inosinate dehydrogenase inhibitor: DT, drug

therapy

inosinate dehydrogenase inhibitor: PD,

pharmacology

serine proteinase: EC, endogenous compound
RNA polymerase: EC, endogenous compound
helicase: EC, endogenous compound
ribozyme: EC, endogenous compound
recombinant alpha2a interferon: CM, drug

comparison

recombinant alpha2a interferon: DO, drug dose
recombinant alpha2a interferon: DT, drug therapy
recombinant alpha2a interferon: PD, pharmacology
recombinant alpha2a interferon: SC, subcutaneous

drug

administration
recombinant alpha2b interferon: CM, drug

comparison

recombinant alpha2b interferon: DO, drug dose
recombinant alpha2b interferon: DT, drug therapy
recombinant alpha2b interferon: PD, pharmacology
recombinant alpha2b interferon: SC, subcutaneous

drug

administration
consensus interferon: CM, drug comparison
consensus interferon: DO, drug dose
consensus interferon: DT, drug therapy
consensus interferon: PD, pharmacology
consensus interferon: SC, subcutaneous drug

administration

peginterferon alpha2b: CT, clinical trial
peginterferon alpha2b: CB, drug combination
peginterferon alpha2b: CM, drug comparison
peginterferon alpha2b: DO, drug dose
peginterferon alpha2b: DT, drug therapy
peginterferon alpha2b: PD, pharmacology
peginterferon alpha2a: CT, clinical trial
peginterferon alpha2a: CB, drug combination
peginterferon alpha2a: CM, drug comparison
peginterferon alpha2a: DO, drug dose
peginterferon alpha2a: DT, drug therapy
peginterferon alpha2a: PD, pharmacology
levovirin: CT, clinical trial
levovirin: AN, drug analysis
levovirin: CM, drug comparison

levovirin: DV, drug development
levovirin: DO, drug dose
levovirin: DT, drug therapy
levovirin: PD, pharmacology
viramidine: CT, clinical trial
viramidine: AN, drug analysis
viramidine: CM, drug comparison
viramidine: DV, drug development
viramidine: DO, drug dose
viramidine: DT, drug therapy
viramidine: PD, pharmacology
merimepodib: CT, clinical trial
merimepodib: AN, drug analysis
merimepodib: CB, drug combination
merimepodib: CM, drug comparison
merimepodib: DV, drug development
merimepodib: DT, drug therapy
merimepodib: PD, pharmacology
thymosin alpha1: CT, clinical trial
thymosin alpha1: AN, drug analysis
thymosin alpha1: CB, drug combination
thymosin alpha1: DV, drug development
thymosin alpha1: DO, drug dose
thymosin alpha1: DT, drug therapy
thymosin alpha1: PD, pharmacology
thymosin alpha1: SC, subcutaneous drug

administration

amantadine: CT, clinical trial
amantadine: AN, drug analysis
amantadine: CB, drug combination
amantadine: CM, drug comparison
amantadine: DV, drug development
amantadine: PD, pharmacology
recombinant interleukin 12: CT, clinical trial
recombinant interleukin 12: AN, drug analysis
recombinant interleukin 12: CB, drug combination
recombinant interleukin 12: CM, drug comparison
recombinant interleukin 12: DV, drug development
recombinant interleukin 12: DO, drug dose
recombinant interleukin 12: DT, drug therapy
recombinant interleukin 12: PD, pharmacology
histamine: CT, clinical trial
histamine: AN, drug analysis
histamine: CB, drug combination
histamine: DV, drug development
histamine: DT, drug therapy
histamine: PD, pharmacology
gamma interferon: CT, clinical trial
gamma interferon: AN, drug analysis
gamma interferon: CB, drug combination
gamma interferon: DV, drug development
gamma interferon: DT, drug therapy
gamma interferon: PD, pharmacology
proteinase inhibitor: CT, clinical trial
proteinase inhibitor: DO, drug dose
proteinase inhibitor: PD, pharmacology
proteinase inhibitor: PO, oral drug

administration

biln 2061: CT, clinical trial
biln 2061: DO, drug dose
biln 2061: PD, pharmacology
biln 2061: PO, oral drug administration
peptide derivative: AN, drug analysis
peptide derivative: DV, drug development
peptide derivative: PD, pharmacology
peptide alpha keto acid: AN, drug analysis
peptide alpha keto acid: DV, drug development
peptide alpha keto acid: PD, pharmacology
pyrrolidine derivative: AN, drug analysis
pyrrolidine derivative: DV, drug development
pyrrolidine derivative: PD, pharmacology
pyrrolidine 5,5 lactam: AN, drug analysis
pyrrolidine 5,5 lactam: DV, drug development
pyrrolidine 5,5 lactam: PD, pharmacology
IDdb3: DV, drug development
IDdb3: PD, pharmacology
unindexed drug
unclassified drug
isis 14803
gw 3112
gw 2549
gw 0569
n [4 [[[6,7 dihydro 2 (4 methylphenyl) 5h

benzocyclohepten

8 yl]carbonyl]amino]benzyl] n,n dimethyl 2h

tetrahydropyran

4 aminium chloride
1,1' [1,4 phenylenebis(methylene)]bis(1,4,8,11 tetraazacyclotetradecane)

CAS REGISTRY NO.:

(ribavirin) 36791-04-5; (serine proteinase)

37259-58-8;

(RNA polymerase) 9014-24-8; (helicase) 42613-29-

6;

(recombinant alpha2b interferon) 98530-12-2;

(peginterferon

alpha2b) 215647-85-1; (peginterferon alpha2a)

198153-51-4;

(merimepodib) 198821-22-6, 198821-38-4; (thymosin

alpha1)

69521-94-4; (amantadine) 665-66-7, 768-94-5;

(histamine)

51-45-6, 56-92-8, 93443-21-1; (gamma interferon)

[4 [[[6,7

82115-62-6; (proteinase inhibitor) 37205-61-1; (n

dihydro 2 (4 methylphenyl) 5h benzocyclohepten 8

tetrahydropyran 4

yl]carbonyl]amino]benzyl] n,n dimethyl 2h

aminium chloride) 229005-80-5; (1,1' [1,4

phenylenebis(methylene)]bis(1,4,8,11

tetraazacyclotetradecane)) 155148-31-5

CHEMICAL NAME:

(1) Vx 497; (2) Ceplene; (3) Biln 2061; (4) Isis

779; Amd

14803; Zadaxin; Gw 3112; Gw 2549; Gw 0569; Tak

3100; IDdb3

```
COMPANY NAME:          (1) Vertex (United States); (2) Maxim; (3)
Boehringer
                       Ingelheim; (4) Isis (United States); Ribapharm;
Merck
                       (United States); Glaxo SmithKline (United
Kingdom); Bristol
                       Myers Squibb (United States); Celera (United
States);
                       Viropharma; Japanese tobacco; IRBM


=> d his

     (FILE 'HOME' ENTERED AT 14:24:22 ON 26 OCT 2004)

     INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE,
AQUALINE,
     AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS, BIOTECHABS,
BIOTECHDS,
     BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN,
CONFSCI, CROPB,
     CROPU, DDFB, DDFU, DGENE, DISSABS, ...' ENTERED AT 14:25:23 ON
26 OCT 2004

     FILE 'REGISTRY' ENTERED AT 14:26:32 ON 26 OCT 2004
L1             1 S 300832-84-2/RN
                 SET SMA OFF
                 DEL SEL Y
                 SEL RN
                 SET SMA LOGIN

     INDEX 'BEILSTEIN, GMELIN' ENTERED AT 14:27:43 ON 26 OCT 2004
                 SEA E1 AND OPTICAL?/FA
                 ---------
L2               QUE 300832-84-2/BI AND OPTICAL?/FA
                 ---------

     FILE 'CAPLUS' ENTERED AT 14:28:02 ON 26 OCT 2004
L3             0 S L1/BMF

     FILE 'CAPLUS' ENTERED AT 14:28:18 ON 26 OCT 2004
L4             0 S L1/BPN

     FILE 'CAPLUS' ENTERED AT 14:28:28 ON 26 OCT 2004
L5             0 S L1/IMF

     FILE 'CAPLUS' ENTERED AT 14:28:41 ON 26 OCT 2004
L6             1 S L1/PEP

     FILE 'CAPLUS' ENTERED AT 14:29:30 ON 26 OCT 2004
L7             0 S L1/PUR

     FILE 'CAPLUS' ENTERED AT 14:29:48 ON 26 OCT 2004
L8             6 S (L1/SPN OR L1/CPN)
L9             6 FOCUS L8 1-

     FILE 'REGISTRY' ENTERED AT 14:31:45 ON 26 OCT 2004

     FILE 'HCAPLUS' ENTERED AT 14:32:46 ON 26 OCT 2004
L10           15 S L1
L11            0 L10 AND CRYSTAL
L12            0 L10 AND CRYSTAL?
L13            0 L10 AND ALCOHOL
L14            3 L10 AND PD<20030327

     FILE 'HOME' ENTERED AT 14:39:45 ON 26 OCT 2004

     INDEX '1MOBILITY, 2MOBILITY, ABI-INFORM, ADISCTI, AEROSPACE,
AGRICOLA,
     ALUMINIUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE,
BABS,
     BIBLIODATA, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS,
BIOTECHABS,
     BIOTECHDS, BIOTECHNO, BLLDB, CABA, CANCERLIT, ...' ENTERED AT
15:24:55 ON
     26 OCT 2004
                 SEA BILN 2061
                 ---------
                 2   FILE ADISCTI
                 1   FILE BABS
                 2   FILE BIOENG
                18   FILE BIOSIS
                 8   FILE BIOTECHNO
                10   FILE CAPLUS
                 2   FILE CBNB
                 1   FILE CIN
                 2   FILE COMPENDEX
                10   FILE DDFU
                10   FILE DRUGU
                 1   FILE EMBAL
                42   FILE EMBASE
                 3   FILE ESBIOBASE
                 1   FILE IFIPAT
                 3   FILE IMSDRUGNEWS
                15   FILE INVESTEXT
                 4   FILE LIFESCI
                13   FILE MEDLINE
                 3   FILE NLDB
                 4   FILE PASCAL
                11   FILE PCTFULL
                 2   FILE PHIN
                 1   FILE PROMT
                22   FILE SCISEARCH
                 4   FILE TOXCENTER
                 6   FILE USPATFULL
                 2   FILE WPIDS
                 2   FILE WPINDEX
L15              QUE BILN 2061
                 ---------

     INDEX 'EMBASE, SCISEARCH, BIOSIS, INVESTEXT, MEDLINE, PCTFULL,
CAPLUS,
     DDFU, DRUGU, BIOTECHNO, USPATFULL, LIFESCI, PASCAL, TOXCENTER,
ESBIOBASE,
     IMSDRUGNEWS, NLDB, ADISCTI, BIOENG, CBNB, COMPENDEX, PHIN,
WPIDS,
     WPINDEX, BABS, CIN, EMBAL, IFIPAT, PROMT' ENTERED AT 15:26:20 ON
26 OCT
     2004
                 SEA L15 AND CRYSTAL?
                 ---------
                 4   FILE EMBASE
                 3   FILE SCISEARCH
                 9   FILE PCTFULL
                 3   FILE BIOTECHNO
                 6   FILE USPATFULL
L16              QUE L15 AND CRYSTAL?
                 ---------

     FILE 'EMBASE, SCISEARCH, BIOTECHNO, PCTFULL, USPATFULL' ENTERED
AT
     15:27:48 ON 26 OCT 2004
L17            0 L16, DUP REM
L18           25 L16
L19           21 DUP REM L18 (4 DUPLICATES REMOVED)
L20            2 L19 AND PD<20030327

=> stnindex
ENTER FILE OR CLUSTER NAMES (NONE):all
FILE 'ENCOMPLIT' ACCESS NOT AUTHORIZED
FILE 'ENCOMPLIT2' ACCESS NOT AUTHORIZED
FILE 'ENCOMPPAT' ACCESS NOT AUTHORIZED
FILE 'ENCOMPPAT2' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS                          SINCE FILE
TOTAL
                                                   ENTRY
SESSION
FULL ESTIMATED COST                                16.52
112.45

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE
TOTAL
                                                   ENTRY
SESSION
CA SUBSCRIBER PRICE                                 0.00
4.90

INDEX '1MOBILITY, 2MOBILITY, ABI-INFORM, ADISCTI, AEROSPACE,
AGRICOLA,
      ALUMINIUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE,
BABS,
      BIBLIODATA, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS,
BIOTECHABS,
      BIOTECHDS, BIOTECHNO, BLLDB, CABA, CANCERLIT, ...'
ENTERED AT 15:32:46 ON 26 OCT 2004

143 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> ciluprevir/cn
FILE '1MOBILITY'
'CN' IS NOT A VALID FIELD CODE
                0 CILUPREVIR/CN
FILE '2MOBILITY'
'CN' IS NOT A VALID FIELD CODE
                0 CILUPREVIR/CN
FILE 'ABI-INFORM'
                0 CILUPREVIR/CN
FILE 'ADISCTI'
'CN' IS NOT A VALID FIELD CODE
                0 CILUPREVIR/CN
FILE 'AEROSPACE'
'CN' IS NOT A VALID FIELD CODE
                0 CILUPREVIR/CN
FILE 'AGRICOLA'
                0 CILUPREVIR/CN
FILE 'ALUMINIUM'
'CN' IS NOT A VALID FIELD CODE
                0 CILUPREVIR/CN
FILE 'ANABSTR'
                0 CILUPREVIR/CN
                0 CILUPREVIR/CN
FILE 'ANTE'
'CN' IS NOT A VALID FIELD CODE
                0 CILUPREVIR/CN
FILE 'APOLLIT'
'CN' IS NOT A VALID FIELD CODE
                0 CILUPREVIR/CN
FILE 'AQUALINE'
'CN' IS NOT A VALID FIELD CODE
                0 CILUPREVIR/CN
FILE 'AQUASCI'
'CN' IS NOT A VALID FIELD CODE
                0 CILUPREVIR/CN
FILE 'AQUIRE'
                0 CILUPREVIR/CN
FILE 'BABS'
'CN' IS NOT A VALID FIELD CODE
                0 CILUPREVIR/CN
FILE 'BIBLIODATA'
'CN' IS NOT A VALID FIELD CODE
                0 CILUPREVIR/CN
FILE 'BIOBUSINESS'
                0 CILUPREVIR/CN
FILE 'BIOCOMMERCE'
'CN' IS NOT A VALID FIELD CODE
                0 CILUPREVIR/CN
<------User Break------>

'CN' IS NOT A VALID FIELD CODE
                0 CILUPREVIR/CN
FILE 'BIOSIS'
                0 CILUPREVIR/CN
SEARCH ENDED BY USER
FILE 'BIOTECHABS'
SEARCH ENDED BY USER
```

```
=> ciluprevir/
FILE '1MOBILITY'
'CILUPREVIR/' IS NOT A VALID FIELD CODE
For a list of field codes for the current file, enter "HELP SFIELDS"
at an arrow prompt (=>).

=> ciluprevir
FILE '1MOBILITY'
             0 CILUPREVIR
             0 CILUPREVIR
FILE '2MOBILITY'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'ABI-INFORM'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'ADISCTI'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'AEROSPACE'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'AGRICOLA'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'ALUMINIUM'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'ANABSTR'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'ANTE'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'APOLLIT'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'AQUALINE'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'AQUASCI'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'AQUIRE'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'BABS'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'BIBLIODATA'
             0 CILUPREVIR
FILE 'BIOBUSINESS'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'BIOCOMMERCE'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'BIOENG'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'BIOSIS'
             0 CILUPREVIR
             0 CILUPREVIR
FILE 'BIOTECHABS'
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L21  QUE CILUPREVIR

=> d rank
F1            3   EMBASE
F2            2   ESBIOBASE
F3            2   MEDLINE
F4            2   SCISEARCH
F5            1   DDFU
F6            1   DRUGU


=> fil f1-6
COST IN U.S. DOLLARS                          SINCE FILE
TOTAL
                                                   ENTRY
SESSION
FULL ESTIMATED COST                                5.70
118.15

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE
TOTAL
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SESSION
CA SUBSCRIBER PRICE                                0.00
4.90

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L22          10 L21

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'20030327' NOT A VALID FIELD CODE
'20030327' NOT A VALID FIELD CODE
L23           1 L22 AND PD<20030327

=> d l23

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     on STN
AN   2004039472  EMBASE  Full-text
TI   Gateways to Clinical Trials.
AU   Bayes M.; Rabasseda X.; Prous J.R.
CS   M. Bayes, Prous Science, S.A., P.O. Box 540, 08080 Barcelona,
Spain.
     mbayes@prous.com
SO   Methods and Findings in Experimental and Clinical Pharmacology,
(
     2003) 25/10 (831-855).
     Refs: 145
     ISSN: 0379-0355  CODEN: MFEPDX
CY   Spain
DT   Journal; General Review
FS   030      Pharmacology
     037      Drug Literature Index
     038      Adverse Reactions Titles
LA   English
SL   English


=> FIL STNGUIDE
COST IN U.S. DOLLARS                                SINCE FILE
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SESSION
FULL ESTIMATED COST                                    8.37
126.52

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE
TOTAL                                                  ENTRY

SESSION
CA SUBSCRIBER PRICE                                    0.00

4.90

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LAST RELOADED: Oct 22, 2004 (20041022/UP).

=> l23 all
MISSING OPERATOR L23 ALL
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> d l23 all
YOU HAVE REQUESTED DATA FROM FILE 'EMBASE' - CONTINUE? (Y)/N:y


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     on STN
AN   2004039472  EMBASE  Full-text
TI   Gateways to Clinical Trials.
AU   Bayes M.; Rabasseda X.; Prous J.R.
CS   M. Bayes, Prous Science, S.A., P.O. Box 540, 08080 Barcelona,
Spain.
     mbayes@prous.com
SO   Methods and Findings in Experimental and Clinical Pharmacology,
(
     2003) 25/10 (831-855).
     Refs: 145
     ISSN: 0379-0355  CODEN: MFEPDX
CY   Spain
DT   Journal; General Review
FS   030      Pharmacology
     037      Drug Literature Index
     038      Adverse Reactions Titles
LA   English
SL   English
AB   Gateways to Clinical Trials is a guide to the most recent
     clinical trials in current literature and congresses. The data
     in the following tables has been retrieved from the Clinical
     Studies Knowledge Area of Prous Science Integrity®, the drug
     discovery and development portal, http://integrity.prous.com.
     This issue focuses on the following selection of drugs: Abetimus
     sodium, adalimumab, alefacept, alemtuzumab, almotriptan, AMGN-
     0007, anakinra, anti-CTLA-4 Mab, L-arginine hydrochloride,
     arzoxifene hydrochloride, astemizole, atazanavir sulfate,
     atlizumab; Belimumab, BG-9928, binodenoson, bosentan, botulinum
     toxin type B, bovine lactoferrin, BufferGel; Caspofungin
     acetate, ciclesonide, cilomilast, ciluprevir, clofarabine, CVT-
     3146; Darbepoetin alfa, desloratadine, diflomotecan, doripenem,
     dronedarone hydrochloride, drotrecogin alfa (activated), DT388-
     GM-CSF, duloxetine hydrochloride, E-5564, efalizumab,
     enfuvirtide, esomeprazole magnesium, estradiol acetate, ETC-642,
     exenatide, exisulind, ezetimib; Febuxostat; Gallium maltolate,
     ganirelix acetate, garenoxacin mesilate, gefitinib; H11, HuMax-
     IL-15, IDD-1, IGIV-C, imatinib mesylate, ISIS-14803, ITF-1697,
     ivabradine hydrochloride; KRN-5500; L-365260, levetiracetam,
     levosimendan, licofelone, linezolid, LJP-1082, lopinavir
     lumiracoxib; MCC-478, melatonin, morphine hydrochloride,
     morphine-6-glucuronide, moxidectin; N-Acetylcarnosine,
     natalizumab, NM-702, NNC-05-1869, NSC-703940; Ocinaplon OM-89,
     omalizumab, omeprazole/sodium bicarbonate, OPC-28326,
     ospemifene; PEG-filgrastim peginterferon alfa-2a, pegsunercept,
     pirfenidone, pralmorelin, pregabalin; Recombinant glucagon-like
     peptide-1 (7-36) amide, repifermin, RSD-1235; S-8184,
     selodenoson, sodium dichloroacetate, suberanilohydroxamic acid;
     TAS-102, terfenadine, teriparatide, tipranavir troxacitabine;
     Ximelagatran; YM-337. .COPYRGT. 2003 Prous Science. All rights
     reserved.
CT   Medical Descriptors:
     *drug monitoring
     drug indication
     drug efficacy
     drug safety
     side effect: SI, side effect
     patient compliance
     drug tolerability
     liver toxicity: SI, side effect
     bleeding: SI, side effect
     disease exacerbation
     systemic lupus erythematosus: SI, side effect
     digestive system ulcer: SI, side effect
     neutropenia: SI, side effect
     teratogenicity: SI, side effect
     human
     clinical trial
     review
     Drug Descriptors:
     abetimus: CT, clinical trial
     abetimus: IV, intravenous drug administration
     adalimumab: AE, adverse drug reaction
     adalimumab: CT, clinical trial
     linezolid: CT, clinical trial
     alemtuzumab: CT, clinical trial
     ivabradine: CT, clinical trial
     ivabradine: IV, intravenous drug administration
     recombinant interleukin 1 receptor blocking agent: CT, clinical
trial
     recombinant interleukin 1 receptor blocking agent: IA,
intraarterial drug
     administration
     glucagon like peptide 1: CT, clinical trial
     glucagon like peptide 1: SC, subcutaneous drug administration
     astemizole: CT, clinical trial
     atazanavir: CT, clinical trial
     bosentan: CT, clinical trial
     botulinum toxin B: CT, clinical trial
     caspofungin: CT, clinical trial
     ciclesonide: CT, clinical trial
     cilomilast: CT, clinical trial
     efalizumab: CT, clinical trial
     imatinib: CT, clinical trial
     terfenadine: CT, clinical trial
     tipranavir: CT, clinical trial
     tipranavir: PO, oral drug administration
     ximelagatran: CT, clinical trial
     ximelagatran: PO, oral drug administration
     ym 337: CT, clinical trial
     moxidectin: CT, clinical trial
     estradiol: CT, clinical trial
     novel erythropoiesis stimulating protein: CT, clinical trial
     novel erythropoiesis stimulating protein: IV, intravenous drug
     administration
     novel erythropoiesis stimulating protein: SC, subcutaneous drug
     administration
     desloratadine: CT, clinical trial
     desloratadine: PO, oral drug administration
     diflomotecan: CT, clinical trial
     diflomotecan: IV, intravenous drug administration
     diflomotecan: PO, oral drug administration
     morphine: CT, clinical trial
     etiracetam: CT, clinical trial
     doripenem: CT, clinical trial
     duloxetine: CT, clinical trial
     unindexed drug
RN   (abetimus) 167362-48-3, 169147-32-4; (adalimumab) 331731-18-1;
(linezolid)
     165800-03-3; (alemtuzumab) 216503-57-0; (ivabradine) 148849-67-
6,
     148870-80-8, 155974-00-8; (glucagon like peptide 1) 89750-14-1;
     (astemizole) 68844-77-9; (atazanavir) 198904-31-3; (bosentan)
147536-97-8,
     157212-55-0; (caspofungin) 189768-38-5; (ciclesonide) 126544-47-
6;
     (cilomilast) 153259-65-5; (efalizumab) 214745-43-4; (imatinib)
     152459-95-5, 220127-57-1; (terfenadine) 50679-08-8; (tipranavir)
     174484-41-4; (ximelagatran) 192939-46-1, 260790-58-7;
(moxidectin)
     113507-06-5; (estradiol) 50-28-2; (desloratadine) 100643-71-8;
     (diflomotecan) 220997-97-7; (morphine) 52-26-6, 57-27-2;
(etiracetam)
     102767-28-2, 33996-58-6; (doripenem) 148016-81-3; (duloxetine)
     116539-59-4, 136434-34-9
CN   Ym 337


=> DIS HIST

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     INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE,
AQUALINE,
     AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS, BIOTECHABS,
BIOTECHDS,
     BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN,
CONFSCI, CROPB,
     CROPU, DDFB, DDFU, DGENE, DISSABS, ...' ENTERED AT 14:25:23 ON
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26 OCT 2004

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                 DEL SEL Y
                 SEL RN
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L2               QUE 300832-84-2/BI AND OPTICAL?/FA
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L3             0 S L1/BMF

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L4             0 S L1/BPN

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L5             0 S L1/IMF

     FILE 'CAPLUS' ENTERED AT 14:28:41 ON 26 OCT 2004
L6             1 S L1/PEP

     FILE 'CAPLUS' ENTERED AT 14:29:30 ON 26 OCT 2004
L7             0 S L1/PUR

     FILE 'CAPLUS' ENTERED AT 14:29:48 ON 26 OCT 2004
L8             6 S (L1/SPN OR L1/CPN)
L9             6 FOCUS L8 1-

     FILE 'REGISTRY' ENTERED AT 14:31:45 ON 26 OCT 2004

     FILE 'HCAPLUS' ENTERED AT 14:32:46 ON 26 OCT 2004
L10           15 S L1
L11            0 L10 AND CRYSTAL
L12            0 L10 AND CRYSTAL?
L13            0 L10 AND ALCOHOL
L14            3 L10 AND PD<20030327

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AGRICOLA,
     ALUMINIUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE,
BABS,
     BIBLIODATA, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS,
BIOTECHABS,
     BIOTECHDS, BIOTECHNO, BLLDB, CABA, CANCERLIT, ...' ENTERED AT
15:24:55 ON
     26 OCT 2004
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                 2   FILE ADISCTI
                 1   FILE BABS
                 2   FILE BIOENG
                18   FILE BIOSIS
                 8   FILE BIOTECHNO
                10   FILE CAPLUS
                 2   FILE CBNB
                 1   FILE CIN
                 2   FILE COMPENDEX
                10   FILE DDFU
                10   FILE DRUGU
                 1   FILE EMBAL
                42   FILE EMBASE
                 3   FILE ESBIOBASE
                 1   FILE IFIPAT
                 3   FILE IMSDRUGNEWS
                15   FILE INVESTEXT
                 4   FILE LIFESCI
                13   FILE MEDLINE
                 3   FILE NLDB
                 4   FILE PASCAL
                11   FILE PCTFULL
                 2   FILE PHIN
                 1   FILE PROMT
                22   FILE SCISEARCH
                 4   FILE TOXCENTER
                 6   FILE USPATFULL
                 2   FILE WPIDS
                 2   FILE WPINDEX
L15              QUE BILN 2061
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     INDEX 'EMBASE, SCISEARCH, BIOSIS, INVESTEXT, MEDLINE, PCTFULL,
CAPLUS,
     DDFU, DRUGU, BIOTECHNO, USPATFULL, LIFESCI, PASCAL, TOXCENTER,
ESBIOBASE,
     IMSDRUGNEWS, NLDB, ADISCTI, BIOENG, CBNB, COMPENDEX, PHIN,
WPIDS,
     WPINDEX, BABS, CIN, EMBAL, IFIPAT, PROMT' ENTERED AT 15:26:20 ON
26 OCT
     2004
                 SEA L15 AND CRYSTAL?
                 ---------
                 4   FILE EMBASE
                 3   FILE SCISEARCH
                 9   FILE PCTFULL
                 3   FILE BIOTECHNO
                 6   FILE USPATFULL
L16              QUE L15 AND CRYSTAL?
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     FILE 'EMBASE, SCISEARCH, BIOTECHNO, PCTFULL, USPATFULL' ENTERED
AT
     15:27:48 ON 26 OCT 2004
L17            0 L16, DUP REM
L18           25 L16
L19           21 DUP REM L18 (4 DUPLICATES REMOVED)
L20            2 L19 AND PD<20030327

     INDEX '1MOBILITY, 2MOBILITY, ABI-INFORM, ADISCTI, AEROSPACE,
AGRICOLA,
     ALUMINIUM, ANABSTR, ANTE, APOLLIT, AQUALINE, AQUASCI, AQUIRE,
BABS,
     BIBLIODATA, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS,
BIOTECHABS,
     BIOTECHDS, BIOTECHNO, BLLDB, CABA, CANCERLIT, ...' ENTERED AT
15:32:46 ON
     26 OCT 2004
                 SEA CILUPREVIR/CN
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                 0*  FILE 2MOBILITY
                 0*  FILE ADISCTI
                 0*  FILE AEROSPACE
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                 1   FILE DDFU
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                 3   FILE EMBASE
                 2   FILE ESBIOBASE
                 2   FILE MEDLINE
                 2   FILE SCISEARCH
L21              QUE CILUPREVIR
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     FILE 'EMBASE, ESBIOBASE, MEDLINE, SCISEARCH, DRUGU' ENTERED AT
15:39:01
     ON 26 OCT 2004
L22           10 S L21
L23            1 L22 AND PD<20030327

     FILE 'STNGUIDE' ENTERED AT 15:40:30 ON 26 OCT 2004

     FILE 'EMBASE' ENTERED AT 15:41:46 ON 26 OCT 2004

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=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS                          SINCE FILE
TOTAL                                            ENTRY

SESSION
FULL ESTIMATED COST                               0.12
130.58

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE
TOTAL                                            ENTRY

SESSION
CA SUBSCRIBER PRICE                               0.00      -
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STN INTERNATIONAL LOGOFF AT 15:42:43 ON 26 OCT 2004
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Session 2A: Keynote lecture. The discovery of **BILN 2061**, an NS3 protease inhibitor with antiviral effects in humans infected with hepatitis C virus. ...
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... **BILN 2061** Establishes Proof-of-Concept in Humans for an HCV Protease Inhibitor ... Note: **BILN 2061** is in clinical development by Boehringer Ingelheim. 10/29/03. ...
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Clinical Care Options for Hepatitis - **BILN 2061** Inhibits HCV ...
BILN 2061 Inhibits HCV Genotype 2 and 3 Proteases in Vitro, ... This study examined the ability of **BILN 2061** to inhibit NS3 protease from genotypes 2 and 3. ...
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BILN 2061 shows promise in early clinical trial against HCV genotype 1, Deanna M. Green, PhD. November 18, 2003 — **BILN 2061** induces ...
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www.medknowledge.de/neu/2002/ IV-2002-32-**biln-2061**-pipeline.htm - 38k - Cached - Similar pages

HIV Report Jan 2003: A Promising New Anti-HCV Protease Inhibitor
... Researchers presented 4 papers describing the discovery, safety and early antiviral activity of **BILN 2061**, a serine protease inhibitor [Hepatology 2002;36:167A ...
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... atilmotin avanafil becatecarin bemotrizinol bisoctrizole canfosfamide hydrochloride cariporide mesylate ciclesonide **ciluprevir** dabuzalgron hydrochloride ...
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... BG-9928, binodenoson, bosentan, botulinum toxin type B, bovine lactoferrin, BufferGel; Caspofungin acetate, ciclesonide,cilomilast, **ciluprevir**, clofarabine, CVT ...
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... TRADEMARK Unknown as yet. MANUFACTURER Boehringer Ingelheim Pharma GmbH & Co. KG. CODE DESIGNATION BILN 2061 ZW. CAS REGISTRY NUMBER **300832-84-2**.
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msdlocal.ebi.ac.uk/docs/exchange/mmcif_rcsb_nmr.dic/ Categories/exptl_crystal_grow_comp.html - 8k - Cached - Similar pages

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CRYSTOOL Move announcement
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(IUCr) **Crystallization** experiments with 2-enoyl-CoA hydratase ...
... Volume 50 Part 4 Pages 443-447 July 1994 **Crystallization** experiments with 2-enoyl-CoA hydratase, using an automated `fast-screening' **crystallization protocol**. ...
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Protein **Crystal** Structure Team I | RIKEN
... (2), Development of high-throughput protein **crystallization protocol** for large scale. (3), Development of in situ X-ray diffractometer for protein **crystal**. image ...
www.riken.go.jp/engn/r-world/ research/lab/harima/group-h/crystal1/ - 12k - Cached - Similar pages

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X-tal **protocols**: References.
... D50, 443-447 **Crystallization** Experiments with 2-Enoyl-CoA Hydratase, Using an Automated 'Fast-Screening' **Crystallization Protocol**. ...
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The Scientist :: **Crystal** Illumination, Jan. 19, 2004
... usually 50 nanoliters, is so crucial to its drug-discovery efforts that the company has patented its proprietary Nano- volume **Crystallization™ protocol**. ...
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